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Physiological Determinants of Aerobic Function in Elderly Males

by

Scott G. Thomas

Department of Physiology

Submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

Faculty of Graduate Studies
The University of Western Ontario
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ABSTRACT

Low cardiorespiratory fitness in the elderly is due to aging and to inactivity. The factors which limit performance of aerobic exercise and which influence the response to a chronic exercise stimulus were examined in a large sample (n=224) of elderly males (mean age 62 years). Men who were retiring from full time employment were recruited and randomly assigned to a training or control group. Maximum oxygen uptake ($\dot{V}O_2max$), pulmonary function and body composition were determined at entry to the study (T1) and one year later (T2). Exercise testing on a motor driven treadmill included a continuous, incremental test (Stage I) and a discontinuous test with three steady state, submaximal, loads concluding with a continuous increase in load to fatigue or symptom limited maximum (Stage II). Cardiac output was estimated with the non-invasive Fick method for CO_2. During the study year control group members were free to pursue their normal activities. The training group exercised (walk/jog) for thirty minutes at approximately 70 percent of the range between maximal and resting heart rates. Supervised training sessions were available thrice weekly.

Results of repeated determinations indicated that maximal oxygen consumption was reliably and reproducibly measured. However, only a minority (1/3) of elderly subjects exhibited a plateau in $\dot{V}O_2$. After one year $\dot{V}O_2max$ was significantly higher in the training group with respect to baseline values (13.2%) and relative to the control group.

The range of response to training was very large and was related more strongly to whether the exercise test was limited by fatigue or symptom limited (eg. electrocardiographic abnormalities, angina) than to training intensity or frequency. Neither cardiac output nor the difference between arterial and venous oxygen contents changed significantly with training. Systolic blood pressure was significantly lower at final testing in both the control and activity groups. The ratio of maximum ventilation during exercise to the estimated maximum voluntary ventilation at rest rose from approximately 80% at baseline to 90% following training. The response to training was smaller in subjects with poor pulmonary function ($FEV_{1.0}$ in lower 40% of sample) versus those with good function ($FEV_{1.0}$ in upper 40%).

Submaximal and maximal responses to training may differ in the elderly. Only a moderate correlation between change in $\dot{V}O_2max$ and training induced bradycardia was observed ($r=0.64$, $p, < 0.05$). The ventilation threshold, which correlates with submaximal exercise performance, was not significantly altered by training which induced a significant increase in $\dot{V}O_2max$.

Maximum aerobic capacity may be influenced by pulmonary function in the elderly. Training can effect substantial increases in capacity but the magnitude of the effect is difficult to predict. The change in maximal oxygen consumption may not be reflected in a submaximal measure such as ventilation threshold. Increased $\dot{V}O_2max$ may be due to a combination of increased cardiac output and oxygen extraction.

ACKNOWLEDGEMENTS

This thesis is based on the Retirement Research Project (Supported by the Ontario Ministry of Health, DM 449). I wish to express my deep felt appreciation to the Research Group, including both my co-workers and the men who were the substance of our research. Seven years of association with David Cunningham has produced two theses, publications, a respect for scientific method and hopefully, an enduring friendship. The role my wife and family have played is more difficult to define simply because it is more pervasive. To them I owe my willingness to sustain the effort required to complete this work.

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CHAPTER ONE

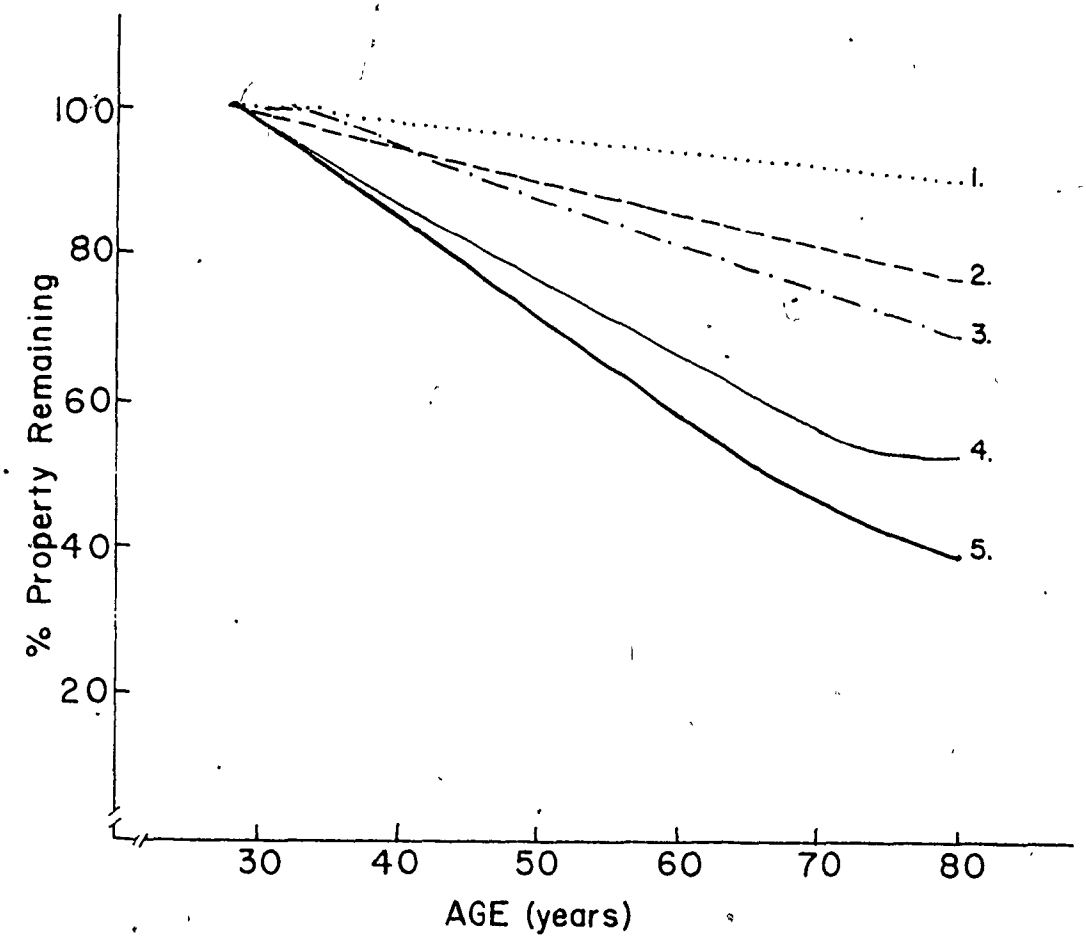
INTRODUCTION

Research designed to identify which physiological factors limit endurance exercise has not resulted in definitive answers but has generated an important body of knowledge about the physiology of the cardiovascular, respiratory and endocrine systems and their interactions. The questions of what factors limit performance of aerobic activities in the elderly has great physiological and practical importance. The aging process has provided physiologists with a profound natural experiment. Since the passage of years affects each of us and each of our physiological systems differently the effect of altering any combination of physiological processes can be determined if a large number of older subjects are examined. The age related alterations also pose a challenge to the control systems of the body. By imposing an exercise stress on elderly subjects we can observe the integrated activity of several physiological systems. The observation of transitions among rest and various exercise intensities may reveal how physiological systems are controlled. Unfortunately, aging is not "clean" experiment. Seldom are all other variables held constant while just one is altered. This difficulty can be partially overcome by utilizing sophisticated data analysis but the problem of confounding variables must be constantly bore in mind in any interpretation of results.

The decline in aerobic exercise performance and its objective measure, maximum oxygen uptake ($\dot{V}O_2max$), is well documented (Astrand et al ., 1973, Bruce, 1984; Dehn and Bruce, 1972; Robinson, 1938; Taylor and Montoye, 1973). However, much less is known about the factors which determine the amount of decline with age which will be observed in an individual. Figure 1 illustrates that the decline in function varies among the components of the gas transport system. These findings suggest that different factors limit oxygen uptake in the elderly compared to young subjects.

The decline in activity level (Cunningham et al., 1968) which accompanies aging influences physiological functions. One method of discriminating a decline in physiological function due simply to aging and one which is related to both aging and decreased physical activity is to impose a chronic exercise stress and thus reverse changes attributable to a less active lifestyle. A number of studies have suggested that the elderly can adjust to chronic exercise with an increase in aerobic exercise performance (Badenhop et al., 1983; DeVries, 1970; Pollock et al., 1976; Sidney and Shephard, 1977). However, all of these earlier studies have methodological or design faults, such as lack of a control group, use of submaximal testing to evaluate changes in maximal function and small sample sizes which

Figure 1. Decline in various physiological capacities and with age. Values at age 25 to 30 are set equal to 100% and the values for older subjects are expressed relative to the values in the young adults. Values are the percent remaining of the original capacity for 1. nerve conduction velocity, 2. maximum heart rate, 3. muscle strength, 4. vital capacity, 5. maximum breathing capacity (Skinner, 1971).



limit the utility of their results. Obtaining samples that are sufficiently large is particular important when studying the elderly because the variability of most physiological measures increases with age (Bafitis et al., 1977. It is not clear whether the magnitude of the response to training and the nature of the physiological adaptation is altered by aging.

The practical importance of examining which factors limit endurance performance can be illustrated by a simple example. The distance across a major intersection is 21.4 meters and the traffic lights allow 35 seconds to cross that distance. Therefore to cross safely, one must travel at 43 meters per minute which is equivalent to an oxygen uptake of 8.7 ml/kg/min. A seventy year old man whose $\dot{V}O_2max$ lies in the bottom quartile of the range in $\dot{V}O_2max$ for his age will require approximately 75 percent of his capacity to cross in the available time. It is crucial to identify the factors which limit his exercise capacity and in addition the determinants of the extent to which that capacity can be improved.

The purposes of this thesis are; 1) to define the reliability of measures of aerobic capacity in the elderly male; 2) to examine the factors which determine the magnitude of the physiological response to training; 3) to investigate the cardiorespiratory factors which limit the ability to respond to acute or chronic exercise in the elderly;

4) to examine the responses of the cardiovascular system to chronic exercise; and 5) to study the rate of response of the gas transport system to a change in exercise intensity in elderly males.

CHAPTER TWO

REVIEW OF LITERATURE

2.1 Factors Limiting Exercise Performance in the Young.

Few investigators have directly studied the factors limiting performance of dynamic exercise in older adults. Studies based on young subjects will serve to introduce the possible mechanisms which limit exercise performance. In section 2.2 the age related physiological changes, which may influence each of the limiting factors, and therefore the ability to perform dynamic exercise, will be considered. Studies using animal models will not be reviewed. This is primarily in the interest of brevity. Data may occasionally be drawn from an animal study if an equivalent investigation of human responses is not available.

The performance of dynamic exercise may be limited by oxygen delivery to the muscles, removal of metabolites, or by the ability of the muscles to use the oxygen delivered. This review concentrates on the mechanisms which may limit oxygen delivery or carbon dioxide removal, primarily because these are the mechanisms which are dealt with in the experimental portion of this thesis. Delivery of oxygen is dependent on ventilation of the alveoli, transfer of gas from the alveoli to the blood, delivery of oxygen saturated blood to the working muscles, and

diffusion of O_2 from blood to the sites of utilization within the muscle fibre. The ability of the muscle to utilize oxygen may be limited by substrate availability, enzyme kinetics or the amount of enzyme present. The role of substrate availability or training induced changes in enzyme kinetics or quantity will not be dealt with. These issues have been reviewed in several publications (Ermini, 1976; Gollnick, 1982; Holloszy, 1976; Suominen, 1977). Blood flow through the working muscle which removes metabolites (lactate, hydrogen ion, carbon dioxide) and respiratory compensation for metabolic acidosis may also indirectly determine the ability of the muscle to generate force (Barclay et al., 1979).

It is important to consider the exercise modality in studies that examine which factors limit dynamic exercise. The two most commonly used instruments are the cycle ergometer and the motor driven treadmill. The highest oxygen consumption on the cycle ergometer is usually 5 to 10% lower than that achieved with treadmill exercise (Astrand and Rodahl, 1977). Subjects who are not accustomed to cycling experience local muscle discomfort in the quadriceps. A peripheral blood flow or oxygen utilization limit is more likely to be observed during cycling because of the smaller muscle mass used in cycling versus treadmill running (Davies and Sargeant, 1975).

2.1.1 The Pulmonary System.

Gas exchange at the lung is not believed to constrain exercise in normal, young subjects. However, definitive experimental evidence on which to base this option is not available for subjects of all ages and levels of training. The respiratory system may fail directly or indirectly to deliver enough oxygen to the blood to meet the demands of dynamic exercise. Indirect failure occurs if the additional oxygen provided by an increase in ventilation is used by the ventilatory muscles (Bye et al., 1983). Failure to oxygenate blood adequately (direct failure) may occur through insufficient ventilation or through inefficiency of gas exchange due to diffusion limitations or ventilation perfusion ratio inequalities.

Estimates of the oxygen cost of high ventilatory levels vary from 0.5 to 1.25 L/min (Bartlett et al., 1958; Bradley and Leith, 1978; McKerrow and Otis, 19560. The work of breathing is a major determinant of the oxygen cost of breathing and therefore of the probability of indirect failure. The work of breathing for high levels of ventilation has been calculated according to the formula $W=bV_E^2 + cV_E^3$ (Otis, where b and c are constants related to the compliance and flow-resistive properties of the respiratory system. Otis estimated that at a critical ventilation of 140 L/min further increases

in $\dot{V}O_2$ would be consumed by the respiratory muscles. Shepherd (1967) studied the O_2 cost of breathing in ten subjects and found the critical ventilation to be 120 L/min. These estimates were made using values of the compliance and flow-resistive properties of O_2 cost of breathing based on studies with young subjects.

Arterial hypoxemia, observed during the performance of high intensity dynamic exercise by athletes, (Dempsey et al., 1984; Gledhill et al., 1980; Rowell et al., 1964) was relieved by hyperventilation consequent to substitution of a helium-oxygen mixture (80:20) for air (Dempsey et al., 1984). The respiratory effort required to produce a given ventilation is decreased when nitrogen is replaced with low density helium because the resistance to flow is reduced. This suggests that respiratory mechanics, or respiratory muscle fatigue may limit minute ventilation, and perhaps oxygen uptake, since reducing the work of breathing produced an increase in ventilation. The hyperventilation usually associated with heavy exercise results in hypocapnia which helps to compensate for metabolic acidosis. An important consequence of the hypoventilation observed during air breathing in Dempsey's studies is a less marked hypocapnia and a decreased arterial pH. Other investigators have not found a significant decrease in arterial oxygen pressure or content during dynamic exercise (Doll, 173; Homgren and Linderholm, 1958).

A respiratory mechanical limit to ventilation should be reflected in the flow-volume loop during exercise. The maximum

flow-volume loop at rest is a description of what inspiratory and expiratory flows can be attained at any lung volume given a maximal ventilatory effort. Inspiratory flow is dependent on airway resistance and the force-velocity characteristics of the inspiratory muscles (Bye et al., 1983). Expiratory flow at or below 60% of vital capacity is not limited by effort but rather by the physical properties of the airways including cross-sectional area and tube compliance (Hyatt 1983). If the flow-volume loop observed during maximal exercise approaches or matches the maximum flow-volume loop observed at rest this would indicate that mechanical factors may be limiting ventilation (Bye et al., 1983). Grimby et al., (1971) and Van Handel (1984) found that athletes attain their maximum flow-volume loops during both the expiratory and inspiratory phases. However, there is evidence that healthy but sedentary individuals do not reach their flow-volume envelopes even during maximal exercise (Grimby, 1971). Jensen and colleagues (1980) concluded that maximal ventilation in exercise by non-athletes is not limited by the mechanical properties of the respiratory pump but that the breathing pattern is influenced by these properties.

Direct failure (arterial hypoxemia) might also result from respiratory muscle fatigue and the subsequent inability to maintain or increase ventilation to match metabolic demand. Evidence that respiratory muscles fatigue with dynamic exercise is based on observations derived from several techniques. The first observation is

that the pressures developed by the inspiratory muscles during exercise exceed those which are known to result in fatigue (Olafsson and Hyatt, 1969; Roussos and Macklem, 1977; Roussos et al., 1979). Martin et al., (1984) found that voluntary isocapnic ventilation at a level matching that achieved in dyanmic exercise increased blood lactate levels (from 0.9 mM/L to 1.8 mM/L). They suggest that lactate accumulation in the respiratory muscles would result in their fatigue. Several authors have found evidence of respiratory muscle fatigue after exercise (Bye et al., 1984; Enoch et al., 1984; Loke et al., 1982). Martin et al., (1982) also demonstrated a decrease in $\dot{V}O_2$max ventilation and heart rate due to fatigue produced by means of prolonged vuluntary hypernea, Finally, the maximum voluntary ventilation which can be be sustained decreases exponentially with the duration of the test (Leith and Bradley, 1976) toward an asymptote of approximately 65 percent of maximum voluntary ventilation at 15 minutes. Ventilation above this level cannot be sustained, which suggests that respiratory muscle fatigue does occur, at least in these special circumstances.

The differences between alveolar and arterial (A-a) oxygen partial pressures increases with exercise intensity (Dempsey et al., 1980). Theoretically this could be due to impairment of oxygen diffusion, ventilation-perfusion inequalities or to shunting of blood away from the lung gas exchange surfaces. The A-a difference reflects some inefficiency in gas exchange and may therefore limit oxygen uptake or

exacerbate a hypoventilatory limit since a larger ventilation is needed to achieve a given quantity of gas exchange. The first possibility to consider is that the transfer of oxygen or carbon dioxide between the alveolus and pulmonary capillary blood is incomplete. A diffusion limitation is reflected in a difference between alveolar and end capillary partial pressures. The transfer of oxygen and carbon dioxide is dependent on the diffusing capacity of the lung, the closely coupled chemical reactions of the gases in the blood and on the time required to traverse the lung capillary bed. Diffusion across the blood-gas barrier is dependent on the pressure gradient from gas to blood and on the area and thickness of the barrier and the diffusibility of the gases in it.

The concentration gradient for O_2 from alveolus to capillary blood increases during exercise as a result of increased alveolar ventilation which increases alveolar PO_2 and decreased PO_2 in mixed venous blood. The area available for gas exchange is increased with exercise due to augmented pulmonary capillary dimensions and recruitment of capillaries which are not perfused at rest (Piiper and Scheid, 1980). The time available for red cell oxygenation is dependent on the ratio of pulmonary capillary volume to pulmonary flow. In an average young adult the volume of blood in the pulmonary capillaries increases approximately three fold, while pulmonary blood flow is increased five fold (from 5 to 25 liters/minute). The result is a decrease in red blood cell transit time from approximately 0.9 to 0.4 seconds, which is still adequate for equilibration of alveolar and pulmonary capillary blood gas pressures

(Dempsey et al., 1980). Dempsey argues however, that capillary transit time may be too brief to allow adequate oxygenation in the athlete whose cardiac output in maximal exercise may reach 35 to 40 liters/minute. This is more probable in the face of the insufficient alveolar ventilation observed in some of these athletes (Dempsey et al., 1982b). This hypothesis has not been experimentally tested.

Mertens (1981) used a mathematical model and found that large alveolar-arterial differences for carbon dioxide did not arise until a severe diffusion impairment was simulated (diffusion factor or capillary transit time less than 10% of normal). He did note that a decreased capillary transit time increased the alveolar-arterial difference for carbon dioxide more if the reaction rate for CO_2 with blood was slow.

Diffusion impairment may result from thickening of the blood-gas barrier. This could occur in exercise if the increase in pulmonary blood flow caused interstitial edema in the lung. There is no evidence that this is a problem in normal subjects. In summary, it appears that diffusion impairment to gas exchange does not occur in healthy young subjects at rest or during exercise.

Inequalities in the distribution of ventilation and perfusion ($\dot{V}/\dot{Q}$) impede gas exchange. Gas exchange units with a large ventilation relative to blood flow have a high alveolar PO_2 and units with a low ratio of ventilation to flow will have a low PO_2 in both air and

blood. Since the PO_2 of the blood is weighted toward the high blood flow units (low $\dot{V}/\dot{Q}$) the arterial PO_2 will be lowered. Similarly alveolar PO_2 will be most influenced by gas exchange units with a high ventilation-perfusion ratio. Approximately 50% of the A-a difference in oxygen partial pressure observed in exercise is believed to be due to inhomogenities in $\dot{V}/\dot{Q}$ (Gledhill et al., 1976). Exercise decreases the inter-regional inhomogenities, which are observed in the resting condition, because increased pulmonary blood pressure, which accompanies exercise, allows better perfusion of the upper regions of the lung (Wagner, 1976). Performing dynamic exercise also increases the overall ventilation perfusion ratio because ventilation increases much more than cardiac output does (Dempsey, 1980). However, the intra-regional $\dot{V}A/\dot{Q}$ distribution becomes less uniform during exercise (Dempsey et al., 1977). Inequalities in the ratio of alveolar ventilation to perfusion decrease the efficiency of ventilation but do not appear to be a major determinant of the maximum gas exchange achieved by healthy, young subjects. An anatomical shunt of 1% or less can account for the remainder of the A-a difference at rest or during exercise in healthy, young subjects (Gledhill et al., 1976). The A-a difference due to shunt increases from approximately 4mmHg at rest to 8mmHg during exercise primarily because of the decreased oxygen saturation of venous blood. Increased shunt of blood during exercise is not a problem in normal young subjects.

In summary, the pulmonary system is not believed to limit gas exchange in sedentary young individuals. There is increasing evidence that it may limit exercise performance in the elite athlete (Bye et al., 1983). This appears to occur because the function of the other components of the gas transport system is improved by training while little change in pulmonary function is produced.

2.1.2 Gas Transport From Blood to Tissue.

The cardiovascular system may impose a limit on the delivery of oxygen and/or the removal of carbon dioxide or other metabolites. Oxygen transport may be limited by the amount of oxygen carried per liter of blood or by the number of liters of blood flow through the exercising muscle (Barclay et al., 1979). Flow through the exercising muscle may be limited either because total blood flow (cardiac output, $\dot{Q}$) is inadequate, because the proportion of blood flow shunted to the muscle is insufficient, or because the ability of the muscle vasculature to accept flow is not great enough (Honig et al., 1980).

A large proportion of the data concerning the role of oxygen delivery in limiting $\dot{V}O_2max$ is derived either from comparisons of very fit and rather unfit subjects (Dempsey et al., 1982; Holmgren and

Astrand, 1966; Keul, 1977; Sjostrand, 1953) or comparisons of measures made before and after exercise training (Clausen, 1977; Scheuer and Tipton, 1977). The studies utilizing the first type of comparison often examine the correlation between $\dot{V}O_2max$ and measures of interest such as total Hb or heart size. The second group of studies are based on the premise that a physiological function which limits oxygen uptake will be improved by training and a function which does not change with training was not a limiting factor. The trouble with this paradigm is that correlation between variables does not define their causal relationship. For example $\dot{V}O_2max$ may increase because maximum stroke volume is larger or stroke volume may reach a new maximum because of an increase in $\dot{V}O_2max$ due to change in another factor. To surmount this problem researchers have attempted to experimentally alter a single component of the gas transport system through manipulations such as induced erythrocythemia, altering the exercising muscle mass or by changing the inspired oxygen concentration.

Systemic oxygen transport is determined by the product of $\dot{Q}$ and arterial oxygen content. The oxygen carrying capacity of the blood is determined by the amount of haemoglobin per erythrocyte and the number of erythrocytes per unit volume of blood. Correlations between total haemoglobin and physical work capacity (Holmgren et al., 1959) have been observed. Experimentally induced erythrocythemia (blood doping) increases maximal oxygen uptake and improves exercise performance (Gledhill, 1982). However, the effect of blood doping may be through

increasing cardiac output. Spriet et al. (1980) in their blood doping study observed a 40% increase in cardiac output determined using dye dilution. They attributed this tremendous increase to improved myocardial function consequent to increased O_2 availability. The change was not due to increased blood volume since maximum cardiac output and $\dot{V}O_2max$ remained elevated after blood volume had returned to control levels (Gledhill, 1982). In contrast, Ekblom et al. (1976) did not observe any change in maximal cardiac output in their study of the effects of blood doping. Total haemoglobin may increase with exercise training (Astrand and Rodahl, 1978) but the results of other studies conflict with this view (Oscai et al., 1968).

During exercise cardiac output may be increased through an increase in heart rate, contractility, end diastolic volume (Frank-Starling mechanism) or a fall in afterload. Each of these variables reaches a limiting value during incremental exercise and may halt the rise in cardiac output. Blomqvist and Saltin (1983) argue that a superior $\dot{V}O_2max$ "requires superior cardiac pump performance". Maximum cardiac output ($\dot{Q}max$) does covary with $\dot{V}O_2max$ (Saltin et al., 1968). The proportion of training induced increase in $\dot{V}O_2max$, which is attributable to a rise in $\dot{Q}$, varies from 100% for subjects who have a high initial level of fitness to approximately 50% for those with a low initial fitness level (Rowell, 1974). The maximum output of the heart is determined by the product of heart rate and stroke volume. Cross-sectional and longitudinal studies have found that maximum heart

rate is either unchanged or reduced following endurance training (Scheuer and Tipton, 1977). Therefore if maximal $\dot{Q}$ is increased in endurance trained subjects the rise must be due exclusively to a larger maximum stroke volume.

The next question that arises is whether the change in maximum stroke volume is due to increased contractility, or increased cardiac dimensions or extramyocardial adaptations that affect the performance of the heart by increasing ventricular filling or decreasing ventricular work. A change in contractility could result from alterations in inotropic factors such as the level of circulating or myocardial catecholamines or from changes in myocardial ATPase, sarcolemmal functional change or an alteration of the proteins which regulate contraction (troponin, tropomyosin) (Penpargkul et al., 1980). Obviously these measures are difficult to make on human volunteers. Only very mild impairment of pump performance during exercise is observed after myocardial contractility is reduced by imposing β-blockade (Port et al., 1980b; Roskamm, 1971). Non-invasive estimates indicate that contractility is not influenced by endurance training (Paulsen et al., 1981; Peronnet et al., 1981).

Results from animal studies suggest that chronic volume loading of the heart may increase ventricular radius and wall thickness (Ross and McCullagh, 1972). Echocardiographically determined cardiac dimensions are larger in endurance athletes (Longhurst et al., 1980; Paulsen et

al., 1981). However, it is not clear whether this is due to long term training or genetic endowment because the findings from longitudinal studies have been less conclusive than the cross-sectional studies. Some longitudinal studies have reported increases in cardiac dimensions with training (DeMaria, 1978; Ehansi, 1978) while others have found no change (Ekblom et al., 1968; Wolfe et al., 1979). Perronet et al., (1981) reviewed the results from both cross-sectional and longitudinal studies of endurance training effects on cardiac dimensions and function. They concluded that although cross-sectional studies demonstrate that endurance athletes have larger left ventricular chambers and a proportional increase in wall thickness longitudinal studies have failed to demonstrate that this increase can be attained through short term (up to 6 months) endurance training.

Clausen (1977) argued that the increase in maximal cardiac output results from both improved myocardial performance and a "locally created ability to reduce the resistance to blood flow in the trained muscles". This reminds us that a change in stroke volume does not necessarily indicate a change in the capacity of the heart pump but may reflect alterations in the after-load and pre-load with which the heart must work. Clausen (1977) in his review of cross-sectional and longitudinal studies of the effect of training noted the inverse relationship between $\dot{V}O_2max$ and systemic peripheral resistance. The lower systemic resistance in the athlete allows a higher cardiac output without producing high arterial pressures. The control of resistance is

primarily at the arterioles through a balance of locally mediated vasodilatory metabolites and adrenergic vasoconstrictor drive. Unfortunately, we have little information about how training may affect arteriolar function.

Several studies have used a single limb training model to elucidate the relative importance of cardiac and peripheral vascular adapations in producing the increased cardiac output which results from endurance training (Davies and Sargeant, 1975; Duner, 1959; Freyschuss and Strandell, 1968; Gleser, 1973; Saltin, 1977; Thomas et al., 1982). This model allows comparison of the response to exercise with trained and untrained limbs but with a common central pump. The difficulty with the model is that one limb training may not provide as large a volume load on the heart as does two limb or swim training. The authors of these studies differ on several points but the overall conclusion is that with this form of training an increase in cardiac output can be achieved without measurable changes in cardiac dimensions or contractility. This suggests that the increase in $\dot{Q}$max is related to improved vascularization of the trained muscle tissue and improved venous return resulting in decreased after-load and increased pre-load. One contrary piece of data comes out of a comparison of the response to arm exercise following leg training. An increase in mean arterial pressure and stroke volume during arm exercise was observed. This finding suggests that myocardial performance may have been improved (Clausen et al., 1973).

The difference between arterial and mixed venous oxygen contents reflects two components, first, the proportion of blood that is shunted to the working muscles, and second, the success of the muscles in extracting oxygen from the blood. The first component is influenced by several other factors including the degree of activation of the autonomic nervous system, which in turn determines the amount of vasoconstriction in inactive tissues, the thermoregulatory demand for flow to the skin, and the degree of vasodilation in the muscle vasculature. The ability of the muscle to extract oxygen is dependent on its capillarization, the transit time through the capillary bed, the gradient in 0_2 pressure from plasma to mitochondria, and the position of the haemoglobin-oxygen dissociation curve. The maximum proportion of available oxygen extracted across exercising muscle is approximately 85%.

A definitive statement regarding the relative importance of peripheral versus central (cardiac) adapatations can not be made since the importance of each component appears to depend on the exercise modality, the amount of muscle tissue employed, and the training state of the individual. However, there is increasing evidence (Thomas et al., 1981; Wolfe et al., 1979) that central adapatations are not as important in the training response to endurance training as peripheral adaptations.

2.2 Age related changes that influence the limiting factors.

2.2.1 The Pulmonary System.

The structure and function of the pulmonary system are markedly altered by the aging process. Each link in the gas exchange process is affected to some degree (Chebotarev et al., 1971). These changes are illustrated by reference to two measures: maximum breathing capacity which declines some 60% with aging (Skinner, 1971) and arterial-alveolar oxygen tension difference at rest which increases from 5.67 mmHg in young subjects to 18.38 mmHg in elderly subjects.

The oxygen cost of breathing in elderly subjects may be increased relative to the young due to changes in the chest wall and lungs. Movement of the rib cage is impeded by kyphosis and by stiffening of the joints (Shephard, 1982). The compliance of the total respiratory system is reduced because the decrease in chest wall compliance is greater than the increase in compliance of the lung (Klocke, 1977). Compliance also decreases with increasing respiratory frequency (LeBlanc et al., 1970; Muiesan et al., 1971). The work of breathing is increased by approximately 20 to 30% between age 20 and age 60 (Milic-Emili et al., 1962; Turner et al., 1968). No estimates of the critical ventilation

(where the oxygen cost of increasing ventilation exceeds the increase in oxygen uptake permitted by augmenting ventilation) appear to exist for the elderly and it is difficult to decide if indirect failure ever occurs in exercise. Assuming the efficiency of breathing remains constant, (it actually decreases) the critical ventilation would be reduced to approximately 90 liters per minute by a 25% increase in the work of breathing.

Partial pressures of oxygen in arterial blood during high intensity exercise by the elderly have not been reported. At rest the arterial PO_2 approximately 0.40 mmHg per year from age 20 to age 70 (Muieson et al., 1971). Julius et al. (1967) reported observing no arterial desaturation in six subjects (50 and 69 years of age) who cycled to a voluntary maximum. However, the low maximum heart rates (mean value 139.6) achieved suggest that the exercise was submaximal. Predicted maximal heart rates for this age group would be 150 to 170 beats/minute. The local fatigue in the leg muscles produced with cycling tends to increase the probability that a peripheral limit to exercise performance will be reached (Davies and Sargeant, 1975). This is particularly true for the elderly subject who may not have experienced cycle exercise for decades. As with the question of indirect failure, lack of data prevents any firm conclusions regarding direct failure. However, we can examine the changes in pulmonary function and structure which predipose the elderly to encountering a mechanical limit to exercise ventilation.

Changes in respiratory mechanics and respiratory muscle function reduce the ventilation that can be achieved by the elderly and decrease the ventilation at which respiratory muscle fatigue is likely to occur. Reductions in maximum expiratory flow at all lung volumes below 70% of vital capacity (Knudson et al., 1977; Turner et al., 1968) and in the volume forcefully expired in 1 second (FEV1.0) are observed with aging (Muiesan et al., 1971). A loss in elastic recoil due to loss of elastic fibres (Klocke, 1977) may underlie the decreases in expiratory flow rate. The effect of changes in respiratory mechanics on the inspiratory phase of ventilation is illustrated by the 28% increase of effective respiratory impedance in the elderly relative to young subjects. Effective respiratory impedance is calculated using the ratio of $P_{0.1}$ to volume inspired/time for inspiration ($P_{0.1}/[Vt/Ti]$). $P_{0.1}$ is an indirect measure of respiratory drive (Rubin et al., 1982) which is determined by occluding inspiration and measuring the pressure generated by the respiratory muscles in the first 100 msec of inspiration. The ratio ($P_{0.1}/[Vt/Ti]$) is an indicator of the amount of respiratory drive required to produce an inspiratory flow. Reports comparing maximal flow-volume loops measured at rest to those attained during exercise for elderly subjects do not appear to exist. The functional result of these decrements in lung function is observed in the decline in maximal voluntary ventilation (approximately 1.5 liters per year) (Muiesan et al ., 1971; Bafitis and Sargent, 1977).

Several factors increase the probability that elderly subjects will experience respiratory muscle fatigue. Fatigue results when the demand placed upon a muscle exceeds its capacity. The factors which determine the demands placed on the inspiratory muscle are: 1. the work of breathing which in turn depends upon the compliance and resistance of the pulmonary system, minute ventilation, and how frequency and tidal volume are combined to achieve a given ventilation ; 2. the strength of the respiratory muscles which is influenced by lung volume (via the length tension relationship or its parallel for respiratory muscles the volume pressure curve), and muscle atrophy. The supply of energy available depends on: 1. the supply of oxygen to the respiratory muscles which is determined by the oxygen content of blood and the amount of blood flow; 2. the force of contraction as a percent of maximum since flow may be occluded by contractions which correspond to a large fraction of the maximum (Macklem, 1980). On the demand side of the ledger we have established that the work of breathing is increased in the elderly (Klocke, 1977) due to decreased compliance and increased resistance of the pulmonary system. The probability of diaphragmatic fatigue is elevated in this age group because the proportion of work done by the diaphragm is increased due to decreased rib cage compliance (Rizzato and Marazini, 1970). The ratio of ventilation to oxygen consumption ($\dot{V}_E/\dot{V}O_2$) is increased in the elderly (Benestad, 1965; DeVries and Adams, 1972; Norris et al., 1955; Patrick et al., 1983) which means that at any $\dot{V}O_2$ the energy demands of the respiratory muscles are increased. The difference in ventilatory cost rises with

$\dot{V}O_2$ reflecting in part the earlier onset of the ventilation threshold (disproportionate increase in ventilation with respect to $\dot{V}O_2$) in the elderly (Thomas et al., 1984). In addition, a larger minute ventilation is required to produce a given amount of alveolar ventilation because of an increase in the size of the dead space (Tenney and Miller, 1966). Despite some contrary findings (Adams et al., 1972; Donevan et al., 1959; the consensus is that ventilation at a given $\dot{V}O2$ is increased with aging (Reddan, 1980).

The combination of tidal volume and frequency selected to achieve a given minute ventilation also affects the energy cost of breathing. During exercise in the young subject, tidal volume and frequency are increased so that the work of breathing (both flow-resistive and elastic) is minimized (Dempsey et al., 1980). Differences in the pattern of increase of tidal volume and frequency which exist between young and old may reflect an attempt by the elderly to adjust to altered pulmonary mechanics. DeVries and Adams (1972) found that the elderly used a large tidal volume and low respiratory frequency to achieve a given level of ventilation. However, the elderly subjects used up their ability to increase tidal volume at relatively low ventilatory levels (approximately 36 liters per minute) and thereafter relied on increasing respiratory frequency. When the tidal volume exceeds 55 to 60% of the vital capacity dyspnea often results (Cotes, 1979). Dyspnea is more likely to occur in the elderly due to the age related decrease in vital capacity.

The strength of the respiratory muscles is decreased in the elderly. The maximum inspiratory and expiratory pressures attained by the elder (55-69yrs) are reduced by approximately 17 and 11% respectively relative to the values for young adults (Black and Hyatt, 1969). The muscles of inspiration are most effective in generating pressure and therefore air movement when the inspiration is originated from a small lung volume (Luce and Culver, 1982). There is a small increase in end expiratory volume with aging but the effect this has on respiratory muscle function is probably slight.

Since the maximum strength of contraction is decreased and the force required to generate a given flow is greater the probability that blood flow in the respiratory muscles may be occluded is heightened. The maximum cardiac output which can be achieved is decreased in the elderly (Shephard and Sidney, 1978). The proportion of this diminished maximal blood flow which is available to the respiratory muscles has not been reported. Arterial PO_2 is decreased at rest in the elderly (Muiesan et al., 1971) but the effect of aging on arterial oxygen content is probably small in mild exercise because there is hemoconcentration with exercise (Doll, 1971). As mentioned earlier little is known about the stability of arterial PO_2 during performance of high intensity exercise by the elderly.

The alveolar-arterial (A-a) difference at rest is increased from approximately 5 mmHg at age 20 to 20 mmHg at age 60 (Mellemgaard, 1966; Muiesan et al., 1971). The alveolar arterial difference is ascribed to 3 components; shunt; diffusion; and distribution inequalities. The proportion of blood flow anatomically shunted is not significantly altered by aging (Bishop and Cole, 1962), however, the effect of a shunt on the alveolar-arterial oxygen tension difference is increased in the elderly because the mixed venous oxygen tension is reduced.

Almost all factors influencing diffusion between lung and blood are altered in the aged. Carbon monoxide (CO) is often used to evaluate diffusion from alveoli to blood. Caution in interpreting results obtained with these techniques is required (Davies, 1982). The steady state method is sensitive to errors in determination of the alveolar tension of carbon monoxide. This is particularly true if the value is calculated from an assumed dead space to tidal volume ratio. The transfer of CO, in contrast to that of oxygen, is comparatively insensitive to pulmonary blood flow rates. Factors affecting the membrane diffusion capacity include the diffusibility of the gas in the membrane, membrane thickness, and the surface area. An electron microscopic study reported that the basement membrane separating capillary blood from alveolar gas is not thickened in samples taken from elderly subjects (Adamson, 1968). In contrast, another author reported that the membrane thickness is increased (Mauderly, 1979). Exercise by the elderly results in a larger increase of pulmonary artery and

pulmonary wedge pressures then is observed in young subjects (Ehrsam et al., 1983; Emirgil et al., 1967). Whether this leads to interstitial or pulmonary edema during exercise in the elderly has not been investigated. The alveolar surface area available for gas exchange is reduced (Pump, 1971; Thurlbeck, 1967).

Hamer (1962) found no significant change in pulmonary blood volume across ages 19 to 59 in a sample of 25 subjects. Other authors have found lower volumes in the elderly (Cotes, 1979, p. 364; Krumholz, 1966). Georges et al. (1978) studied a large sample (n=70) of men (n=47) and women (n=23) who were between 18 and 78 years of age. He observed a steady decline in the diffusing capacity for carbon monoxide from approximately age 40 and a rapid decrease in pulmonary blood volume after age 50. Measurements made at rest in the elderly of diffusion capacity for carbon monoxide (Shephard and Anderson, 1968) show a decrease of 0.07 to 0.08 mM/min/kPa per year between 25 and 65 years of age. This represents approximately a 33% decline between age 20 and 60 (Reddan, 1980). However, some investigators have argued that the decline in diffusion capacity is not responsible for the increase in A-a O_2 tension difference because even marked reductions in diffusing capacity have little effect on the difference (Mellemgaard, 1968).

A diffusion limitation during performance of exercise by the elderly has not been directly investigated. DL,CO is lower in the elderly with respect to the young during sub-maximal exercise (Emirgil

et al., 1967; Hanson and Tabakin, 1964). Cohn and co-workers (1954) found a decrease in diffusing capacity at maximal exercise across age groups but it is argued that the oldest subjects may not have reached a true maximum. Niinimaa and Shephard (1978) found that the diffusing capacity at rest was lower in the elderly but that the increase with exercise was greater in the elderly up to the maximum level observed (approximately 65% of $\dot{V}O_2max$). Their conclusions were weakened by methodological problems including failure to correct for differing haemoglobin values, and assumption of a constant dead space to tidal volume ratio during exercise of increasing intensity (Bradley et al., 1976; Mellemgaard, 1966). In a recent review, Piiper and Scheid (1980) state that the question of whether diffusing capacity rises steadily with exercise intensity is often discussed but that there is insufficient data to resolve the question.

There may be less variation in pulmonary blood flow from apex to base of the lung (Muiesan et al., 1971). This may result from increased pulmonary artery and wedge presssures (Ehrsam et al., 1983). If a larger porportion of the remaining blood vessels are perfused at rest in the elderly it would suggest that pulmonary blood volume may not increase as much with exercise. Oxygenation of the blood or removal of carbon dioxide may not be complete if the transit time through the lung is too brief in relation to the rate of gas exchange.

The transit time of red blood cells through the pulmonary capillary bed has not been studied in elderly subjects. The transit time is dependent, as in the young, on the ratio of pulmonary blood flow to volume. The maximum cardiac output attained in exercise by the elderly is reduced (Hossack et al., 1980) but pulmonary blood volume measures are lacking. The possibility that oxygenation of blood or removal of carbon dioxide is not complete during exercise in the elderly deserves more study.

The most important determinant of the age related increase of the A-a oxygen tension difference is heterogeneity of ventilation/perfusion ratios. The distribution of ratios is more uniform between regions of the lung but this is accompanied by less homogeneous intraregional distribution (Muiesan et al., 1971). This increased dispersion of $\dot{V}/\dot{Q}$ ratios is a factor in the increased physiological dead space observed in the elderly (Tenney and Miller, 1966). Areas of low $\dot{V}A/\dot{Q}$ are present in the lungs of elderly subjects but not in young subjects (Wagner et al., 1976; Piret et al., 1982). It is uncertain whether changes in the distribution of blood flow are important in altering $\dot{V}/\dot{Q}$ ratios in the elderly (Kronenberg et al., 1973; Muiesan et al., 1971; Piret et al., 1982). Distribution of ventilation to individual alveoli is less homogenous. The simplest test of inequality of ventilation distribution is the single breath nitrogen washout. The single breath nitrogen index rises from approximately 0.6% to 1.4% between the ages of 20 and 60 (Cotes, 1979, p. 383). The volume at which bronchioles close during

expiration is increased in the aged (Cotes, 1979, p. 362). This closure may degrade the matching of ventilation and perfusion. The effect of mild exercise on $\dot{V}/\dot{Q}$ in old subjects has been studied by Derks (1980). He found that at rest the elderly subjects exhibited wider dispersions of ventilation and perfusion than did his young subjects. With mild exercise the distribution narrowed in both the young and old but the improvement in the elderly subjects was greater. In discussing the difference between his findings of improved V/Q ratios and those of Gledhill and co-workers (1977) who observed increased heterogeneity with exercise, Derks suggests that the difference may be due to the use of vigorous exercise by Gledhill's group. This must be considered when evaluating what happens to $\dot{V}/\dot{Q}$ ratios during heavy exercise by the elderly.

In addition to the other changes there is a change in the reaction between haemoglobin and oxygen with aging which is reflected in the pressure required to reach 50% saturation of haemoglobin (P50=27.5 mmHg for 18 to 39 year olds, 28.8 for 60 to 69 year olds) (Flenley et al., 1975).

In summary, there are widespread alterations in pulmonary structure and function with aging. These changes reduce the reserve capacity of the pulmonary system. Several critical pieces of data are missing from the present description of the role of the ventilatory system in determining exercise performance in the elderly. In order to define

whether a pulmonary limitation to oxygen uptake is reached in the elderly, information is needed about the oxygen cost of breathing, the arterial blood gas tensions throughout exercise and particularly at maximal exercise, and the flow-volume loops during high intensity dynamic exercise. The incidence of respiratory fatigue during exercise by elderly subjects needs to be objectively quantified and further information concerning A-a differences during exercise of increasing intensity and what factors contribute to the difference are required.

The problem in deciding what limits exercise on the basis of measurements of maximum exercise ventilation and maximum oxygen consumption is to establish causation. Does the subject stop exercise because his ventilation is limiting or is his maximal ventilation limited because he stopped exercise due to variety of other factors? In the absence of the measures listed above an indirect approach to addressing this question must be made. One method is to compare ratios of exercise ventilation to maximum $\dot{V}O_2$ ($\dot{V}_E/\dot{V}O_2$) in young and old. Studies have found that the $\dot{V}_E/\dot{V}O_2$ is increased (Fisher et al., 1965; Greifenstein et al., 1952) which suggests that the elderly may be prone to respiratory muscle fatigue and a mechanical limit to ventilation. Another ratio of interest is the maximum exercise ventilation achieved to the maximum sustained ventilatory capacity. The sustained ventilatory capacity is a measure of the ability to maintain a high level of ventilation for a sustained period and may therefore be a better measure of a subject's ability to maintain adequate ventilation

during prolonged endurance exercise. The ratio of exercise ventilation to sustained ventilatory capacity is increased in the elderly (Belman, 1984) a result which reinforces the conclusion that the ventilatory reserve is reduced with aging.

2.2.2 Aging and O_2 delivery.

Aging strongly influences the function of the gas transport system. The influence of aging alone on the cardiovascular system is confounded by the presence of changes due to deconditioning and disease in a high proportion of elderly subjects (Cunningham et al., 1968; Bruce, 1983). The effect of inactivity may be estimated by cross-sectional analyses of subjects with varying activity levels or preferably by a longitudinal study of the effects of increasing activity. We will examine the results of these studies in section 3.2. The effect of disease may be diminished by pre-screening subjects to remove those with overt signs of cardiovascular disease. However, the marked prevalence of cardiovascular disease in those over age 60 may render this technique impractical. In addition, when a disease of often unknown etiology is present in a large proportion of a population (Taylor and Montoye, 1972; White et al., 1950) it may be more sensible to consider it a normal part of the aging process.

Total haemoglobin, blood volume and the number of red blood cells may be reduced with aging. Shephard (1978, p. 81) suggests that the fall observed in population surveys may reflect poor nutritional status rather than aging per se. The effect of these changes on the oxygen carrying capacity of blood has not been directly studied. Granath et al.

(1964) reports that acute exercise increases the oxygen carrying capacity by approximately 1 volume percent in the elderly. The hypokinetic circulation of the older subject may increase rouleaux formation which exercise disperses. As with young subjects a correlation between total haemoglobin and physical work capacity is observed ($r = 0.385$, $p<0.05$) but since this correlation disappears when haemoglobin is expressed as haemoglogin concentration or as haemoglobin per kilogram of body weight, it appears that the correlation is due to a common relation of physical work capacity and total haemoglobin to body size (Davies, 1972; Ericsson, 1970). In summary, it appears that a slight decrease in the oxygen carrying capacity of blood may occur but primarily because of poor nutrition and that the change in blood volume or total haemoglobin does not account for age related decreases in maximal oxygen consumption.

A reduction in maximal cardiac output, due to decreases in both maximum heart rate and stroke volume, has been consistently suggested in studies of the elderly (Becklake et al., 1965; Hossack and Bruce, 1982; Shephard, 1980). One of the first observations regarding maximal exercise in the elderly was the decrease in maximal heart rate (Master and Oppenheimer, 1929; Robinson, 1938). Several studies have confirmed this finding (Astrand et al., 1973; deVries, 1970; Grimby et al., 1972). Maximal heart rate is often estimated using the formula - Maximum Heart Rate (bpm)=220-age (years). Shephard states that it is now recognized that this formula "underestimates the maximum for sedentary North

Americans". He suggests that previously reported lower maximum heart rate values may have resulted from the investigator's reluctance to push their subjects to a true maximum and that the average maximum for men between ages 65 and 83 is between 170 and 177 beats per minute. Hossack and Bruce (1982) treadmill tested 98 men who were between the ages of 20 and 75 years. The regression formula they developed was Heart Rate= 227-1.067age ($r=-0.63$, $p<0.05$) which for a 65 year old subject predicts a maximum heart rate of 157.6 versus the 155 value obtained from using the old 220 - age formula. However, the mean heart rate for the 50 to 59 year old group (n=28) was 172 $\pm$ 10 and for the 60 to 75 year olds 160 $\pm$ 7 beats per minute. This difference illustrates that fitting a linear regression equation across all age groups may result in poor prediction for any one age group.

Possible explanations of the decreased maximal heart rate are myocardial oxygen lack, decreased myocardial compliance, reduced sympathetic drive to or sensitivity of the cardiac pacemaker, (Shephard, 1978, pp.75-78) or decreased conduction velocity in the heart (Gerstenblith et al., 1976). Studies with adult and senescent beagles (Yin et al., 1979) have demonstrated that the maximal heart rate response to adrenergic stimulation is reduced with increased age. Furthermore, this decrease is not due to inability of the heart to beat at higher rates since the maximal heart rate reached during atrial pacing was approximately double that achieved with adrenergic stimulation. Conway et al. (1971) used β-blockade to determine the

importance of changes in sympathetic drive in setting maximum heart rate. They observed the same heart rate reduction with β-blockade in old and young subjects. The heart rate at a given submaximal load is similar for young and old subjects with variations due to fitness level rather than to aging (Astrand, 1967; Strandell, 1964).

The maximum stroke volume attained during dynamic exercise may be low in the elderly (Hossack et al., 1980). Unfortunately, very few actual measurements of cardiac output at a true maximum oxygen uptake level using old, rather than middle-aged subjects, exist. Hossack et al. (1980) estimated maximal cardiac output for a large number (n=99) of subjects. $\dot{V}O_2max$ was measured and maximum cardiac output was then calculated from a previously determined regression equation which was based on a set of 49 observations made on 10 men whose ages ranged from 20 to 64 years (mean 46.4). Cardiac output was calculated using the direct Fick principle from measurements of arterial and mixed venous oxygen tensions and oxygen uptake. The difficulty during maximal exercise in fulfilling the assumption of steady state required by the Fick equation is not dealt with. It is not clear from the report whether or not submaximal cardiac output and $\dot{V}O_2$ values were used in developing the equation which is used to predict maximal values for cardiac output. The effect of age on maximum cardiac output within this group was reported but not discussed. A strong correlation (r=0.92) between age and maximum cardiac output can be calculated from the data presented in their Table 1. This correlation appears to be due to the

decline in maximum heart rate with increased age since little association between age and stroke volume at maximum cardiac output is observed (r=0.02). The average stroke volume at maximum cardiac output for the eldest 4 subjects (mean age 61.5 years) was 104 ml versus an average of 108 ml for the 4 youngest subjects (mean age 27.0 years).

Conway et al. (1971) used the dye dilution technique to measure cardiac output in young (20-35 years) and old 50-65 years) men during upright cycle ergometer exercise. Stroke volume at the maximum level of exercise averaged 86 ml for the young men and 80 ml in the old subjects. The peak heart rates were slightly below the expected maximum values at 180 and 158 beats per minute in the young and old subjects respectively.

Several studies have examined the pattern of change in stroke volume and the relationship between cardiac output and $\dot{V}O_2$ during submaximal exercise of increasing intensity in middle aged (Hartley et al., 1969; Grimby et al., 1966) and older subjects (Becklake et al., 1965; Granath et al., 1964; Julius et al., 1967; Niinimaa and Shephard, 1978). The relation between cardiac output and stroke volume may indicate whether and how age has altered the cardiovascular system. In young adults stroke volume either increases continuously to maximum $\dot{V}O_2$ or plateaus at approximately 80% of $\dot{V}O_2$max. Varying results have been reported in studies of the elderly but most authors (Granath et al., 1964; Julius et al., 1967) find that the slope of the relation between cardiac output and $\dot{V}O_2$ is the same in young and old subjects

but the $\dot{Q}$ at a given $\dot{V}O_2$ is lower in the elderly due to a smaller stroke volume.

Becklake et al. (1965) used the nitrous oxide method for determining cardiac output which may be unreliable due to difficulty in defining alveolar gas fractions and to recirculation of nitrous oxide. The subjects (n=48) ranged in age from 22-83 years old: the number of subjects in each decade grouping is not reported. A greater rate of rise of cardiac output was found for the older subjects relative to those under age 40. An unusual finding in this study was a lower heart rate at a given work load in the older subjects. Stroke volume was higher in the older subjects. The pattern of change in stroke volume with increasing workload bore no discernible relation to the subject's age. Multiple t-tests were performed to examine differences between decade groupings with no mention of the required correction of the critical t-value. The findings from these comparisons were that cardiac output at a given $\dot{V}O_2$ is higher in the elderly, as is stroke volume.

Granath et al. (1964) used the direct Fick method to compare the circulatory responses of young and old men. The stroke volume for the old men was lower at rest in the supine posture. A lower cardiac output at a given $\dot{V}O_2$ was due to a lower stroke volume. The pattern of increase in stroke volume was similar in the two age groups.

Thirty-five male subjects and 19 women were studied by Julius et al. (1967). Results from subjects of both sexes were grouped together. Eighteen subjects fell into each of three age groupings I: 18-34, II: 35-49, III: 50-69. Cardiac output at rest and during exercise on a cycle ergometer was determined using the dye-dilution technique. The use of this method during exercise has been criticized on the grounds that it overestimates cardiac output and lacks precision (Donald and Yipintsoi, 1973; Hanson and Tabakin, 1964). Cardiac output at a given $\dot{V}O_2$ was lower in the oldest age group (Group III) with respect to the younger two groups. This was also true for stroke volume which leveled off in the two younger age groups but not in the older subjects. The authors suggest that the cardiovascular system does not limit $\dot{V}O_2$max in the eldest subjects since stroke volume and cardiac output do not plateau up to the maximum exercise level completed by their subjects. The average heart rate at the final exercise level was 139.6 beats per minute for the group III members which is approximately 82% of the expected maximum for that age group.

The methods employed by Niinimaa and Shephard (1978) differ from those of studies previously discussed and require some comment since similar methods will be used in the experimental studies described in following sections of this thesis. Cardiac output was calculated using indirect measures of arterial and venous carbon dioxide pressures, direct measurement of $\dot{V}CO_2$ and applying the Fick principle. The venous partial pressure of CO_2 was measured using the Jones rebreathing

method (Jones et al., 1975). Arterial PCO_2 was calculated from end tidal PCO_2 using a regression equation developed by Jones et al. (1979). The use of this equation in the elderly may not be appropriate since it was developed on a small sample of young men and age related changes in the pulmonary system may alter the relationship between end-tidal and alveolar and between alveolar and arterial CO_2 pressures.

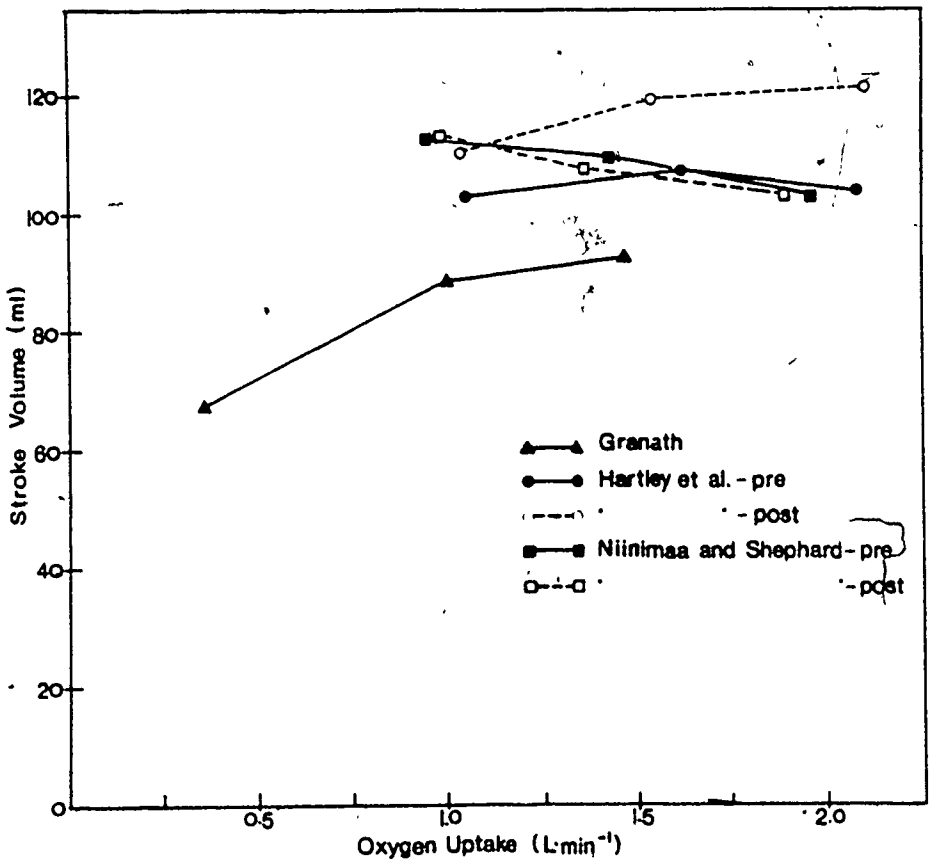
The next difference of note is that Niinimaa and Shephard (1978) used treadmill testing versus cycle ergometry which was utilized in the previous studies. Cardiac output and stroke volume are greater and heart rate is lower at a given $\dot{V}O_2$ during treadmill exercise compared to cycle ergometry. Eight men and 7 women were studied and sex differences in cardiac output and stroke volume were noted. We will consider only the data from the male subjects. The slope of a cardiac output versus $\dot{V}O_2$ plot of their data gives a slope of 3.82 liters of blood flow per liter of oxygen uptake. This is lower than the range of 5.0 to 5.9 observed in other studies which were summarized by Faulkner et al. (1977). Stroke volume dropped from the first to second and more abruptly to the third load in this study. Again this is in opposition to the results of other studies (Granath et al., 1964; Julius et al., 1967).

The results of three studies which published data on stroke volume and oxygen uptake during submaximal exercise are illustrated in Figure 2. The disparity in findings is likely due to the interplay of several

factors; age of the subjects (mean age ranges from 47 to 70); training state; cardiac output measurement technique; and variation in the subject's physiological state due to the presence of disease (cardiovacular or respiratory). The relative importance of these factors is difficult to separate. There is no consistent pattern of change with increasing age over the range available and training appears to alter the absolute values observed rather than the pattern of change. On the basis of their own cardiac output (CO_2 rebreathing) data and a review of the published data Faulkner and his colleaugues (1977) conclude that the relation between $\dot{Q}$ and $\dot{V}O_2$ for physically active men of all ages and all men under age 40 is $\dot{Q}$(ml/kg/min) = $5.2\dot{V}O_2$ + 66 (ml/kg/min). For inactive men over 40 years of age the slope is increased and the intercept decreased ($\dot{Q}=5.9\dot{V}O_2$ + 49).

Despite these disparate findings it appears that stroke volume is reduced by aging at some levels of dynamic exercise. What are the mechanisms responsible for this impairment of function? A change in stroke volume can result from changes in myocardial function (contractility) or from alterations in preload or afterload due to changes in the peripheral vasculature or change in myocardial size. Age related changes in myocardial function will be considered first. Alterations in myocardial function and the underlying cellular mechanisms have been ably reviewed by Lakatta and Yin (1982). A cross-sectional study of the duration of each of the phases of the cardiac cycle in subjects between ages 9 and 97 revealed that at rest

Figure 2. Relation between stroke volume and exercise intensity ($\dot{V}O_2$) observed in several studies from the literature. Mean age of subjects from 47 to 70 years. Values for before and after training are illustrated. Details of experimental protocol and measurement techniques are given in the text.



isovolumic contraction time, duration of ejection and isovolumic relaxation time are all increased (Harrision et al., 1964). The authors emphasize the roughness of their noninvasive measures. The increased time required for ventricular relaxation was more recently confirmed using an echocardiographic measure (Luisada et al., 1975). A group of researchers (Bodurian et al., 1984) have reported on the results obtained from cardiac catheterization data collected over a seven year time span. Two hundred and nineteen normal subjects between the ages of 13 and 79 were studied at rest. Cardiac output was determined with the dye dilution technique, vascular pressures were determined by left heart catheterization and biplane left ventriculography was used to estimate cardiac dimensions. Cardiac index declined after age 40. End diastolic pressure did not change with age, nor did these researchers find any change in left end diastolic volume or ejection fraction. Port et al. (1980) used radionuclide angiocardiography to study left ventricular function at rest and during upright cycle ergometer exercise. The authors carefully screened out those subjects with clinically identifiable cardiovascular disease. They confirmed the data gathered by Bodurain and colleagues but in addition found that in contrast to young subjects the old (60+) fail to increase left ventricular ejection fraction with exercise. Regional contraction abnormalities were found with increasing frequency during exercise in subjects who were 60 years of age or more. No significant changes in end diastolic volume index or peak systolic pressure were found with increasing age. From these findings the authors suggest "that there are no major differences in the

afterload or preload of older subjects" and that there is an age related decline in left ventricular contractile reserve. Lakatta and Yin (1982) suggest, primarily on the basis of animal studies, that a change in myocardial function may result from decreased responsiveness of the heart to catecholamines and that slower removal of calcium by the sarcoplasmic reticulum may contribute to the slower relaxation time. Other workers have found an increased afterload with aging (Gerstenblith et al., 1976; Granath et al., 1970) which is ascribed to the increased stiffness of the vascular bed.

Myocardial hypoxia may limit the performance of the heart. The incidence of electrocardiographic abnormalities (ST segment depression, ectopic beats) may increase with age from approximately 6% in subjects 30 years old to 62% at age 76 (Daly et al., 1968). However, other reports have found a much lower incidence. Lester and colleagues found ST segment depression in approximately 5% of his subjects who were between 40 and 75 years of age. Doan and co-workers (1965) found rates of 24.1 and 46.1 percent in the sixth and seventh decades respectively. A portion of this difference can be ascribed to pre-selection of subjects in Daly's study. Maximal exercise tests are routinely halted because of ECG abnormalities and the use of anti-arrhythmics does allow a higher exercise level to be obtained.

The maximum amount of blood flow is determined by the ratio of maximum mean aortic pressure to minimum total peripheral resistance. A simplistic way of viewing the system is to say that the heart determines the maximum pressure but the ability of peripheral vasculature to dilate determines the minimum resistance. This approach ignores the intricate web of feedback between the two components of the cardiovascular system. The rate pressure product at maximal exercise is unchanged (Sheffield and Roitman, 1973), however the work of the heart is increased due to increased impedance to ejection (Bader, 1967). It has been suggested that the increase in heart mass with age (Strandell, 1964) is a compensatory response to the increased pressure load.

Gerstenblith and his co-authors reviewed the effects of aging on the vasculature. Aging is associated with thickening and stiffening of the larger vessels (Learoyd et al., 1966) and a diminished ability of the aorta to relax following stimulation with isoproterenol (Fleisch et al., 1970). However, data concerning changes at the arteriolar level are missing. The ratio of capillaries to muscle fibres is decreased, although the number of capillaries per square millimeter of muscle tissue is unchanged due to a decrease in average fiber size (Parizkova et al., 1971). The maximum blood flow following ischaemia in the calf muscle is not altered across age groups (Kroese, 1977). The minimum peripheral resistance is larger in the elderly despite a larger fall from the high basal resistance. The conclusion drawn in Gerstenblith's review (Gerstenblith et al., 1976) is still valid today " It is unclear

whether this higher vascular resistance in the elderly is due to decreased vasodilating capacity or decreased stimulus to vasodilation, or due to normal reflex adjustments to a lower capacity of the heart to augment cardiac output." The difference between arterial and mixed venous oxygen content is increased at rest in proportion to the fall in resting cardiac output. The maximum $a-\bar{v}\ O_2$ difference reached during exercise is diminished (Julius et al., 1967; Hartley et al., 1969)). It is not clear whether this is due to a reduced ability of the muscle tissue to extract and utilize oxygen or to a decreased ability to direct flow away from other tissues and therefore a decreased proportion of flow through the high extraction muscle tissue. However, since the arterio venous oxygen content differences are calculated from cardiac output any errors made in the determination of $\dot{Q}$ will be reflected in the $a-\bar{v}\ O_2$ content difference. Shephard (1978) assumes that aging does not alter the proportion of blood flow which goes to the muscles and calculates an $a-\bar{v}\ O_2$ difference across the working muscle of 160 to 170 ml/liter. His assumption is not justified since redirection of blood flow depends on autonomic nervous system function which is known to change with aging (Skinner et al., 1973). The ability of muscle to extract and utilize oxygen may be reduced due to decreases in enzyme activity (Larsson and Karlsson, 1978). However, some authors (Orlander et al., 1978) found that the decrease in $\dot{V}O_2max$ with aging cannot be explained in terms of deteriorating skeletal muscle energy metabolism.

2.2.3 Gas Exchange Kinetics in the Elderly

Aging may influence the rate at which ventilation, heart rate and gas exchange are adjusted to meet the demands of a change in exercise intensity. A slower rate of response would require more anaerobic metabolism. The anaerobiosis would increase production of lactic acid thereby decreasing pH and producing a greater disturbance of homeostasis.

Robinson (1938) noted a slower rate of rise in heart rate in his older subjects. Berg (1947) examined recovery curves for $\dot{V}CO_2$ and $\dot{V}O_2$ after moderate exercise in subjects whose age ranged from 18 to 68 years. Various parameters have been used to decribe the rate of response including half times, time constants, and time to peak response. The Bethesda group (Norris et al., 1955) simply examined the time of maximum response to an increase in load on a cycle ergometer. They found no consistent pattern of change with age. Norris and his co-workers did note that the older subjects responded more slowly than the young subjects to higher intensity exercise. Berg used a semi-logarithmic plot of log gas exchange against time to determine the half time (t1/2) for the recovery. The t1/2 for $\dot{V}CO_2$ correlated with age of the subject ($r=0.75$) while only a weak association between $\dot{V}O_2$ and age was noted ($r=0.43$). Berg notes that the reliability of the $\dot{V}O_2$ t1/2 was low ($r=0.55$). He corrects for the attenuation in correlation this low reliability causes and suggests that the true correlation between age and the t1/2 of $\dot{V}O_2$ is 0.71. The role of differing fitness between his young and old subjects is impossible to evaluate. Increased $\dot{V}O_2$max is

associated with shorter response times in young subjects (Hickson et al., 1978).

DeVries and his co-workers (1981) compared the kinetics of response to step increases to 100 W and 45% of $\dot{V}O_2$max in young (21-29 yrs) and older (60-69 yrs) men (n=10). His older subjects were selected from a group of Senior Olympic endurance competitors. Both young and older subjects were approximately 2 standard deviations above the mean $\dot{V}O_2$max values for their age group. The half time of the response was determined graphically from a semi-log plot of 30 second averages for ventilation and $\dot{V}O_2$. Gas exchange was determined from expired volume (Parkinson-Cowan, CD-4) and mixed expired gas sampled from a mixing box. There are several problems associated with this type of system. The response of the CD-4 dry gas meter is not linear and is further distorted by the moisture from expired gas. Matching of flow to concentration is a problem with this type of system. A fixed time delay between flow and concentration signals of 30 seconds was employed. This may be a source of error since the delay is dependent on the volume of gas ventilated. Calibration of gas exchange was limited to ventilations between 23 and 33 liters per minute. These authors observed no significant delay in the mean t1/2 for steps to 45% of $\dot{V}O_2$max in the young (27.4 sec) and old (30.0 sec). No difference in heart rate kinetics was found. How representative these findings are of differences between young and old is difficult to discern. DeVries et al. (1981) chose very fit subjects from both age groups. The effect of training on

kinetics in the old has not been investigated.

2.3 Physical Training and The Elderly.

2.3.1 Determinants of the training response.

The interactions among age, physical endurance conditioning and physiological function have been explored in several studies (Benestad, 1965; DeVries, 1970; Karsch and Wallace, 1976; Niinimaa and Shephard, 1978; Pollock et al., 1976; Saltin et al., 1969; Seals et al., 1984; Sidney and Shephard, 1978; Suominen et al., 1977; Tzanokoff et al., 1972). Examining these studies may help reveal which factors limit acute exercise and to determine whether aging decreases the ability to respond to the stimulus of chronic exercise by adaptations which increase maximal exercise capacity. A range of increase in $\dot{V}O_2$max from zero (Benestad, 1965) to 38% (Barry et al., 1966) is observed as a result of endurance training programs with elderly participants. Factors which influence the response to a training program in young adults include the subject's initial fitness level, the subject's previous activity levels, the frequency, intensity, and duration of an exercise training session, and the total duration of the conditioning program (Pollock, 1973; Shephard, 1968). The role each of these factors plays in explaining the variability in response to training observed in studies of the elderly will be examined.

Several authors have attempted with little success to determine if the ability to adapt to exercise training is reduced in the elderly (Benestad, 1965; DeVries, 1970; Kilbom, 1971; Pollock, 1973; Sidney and Shephard, 1978; Ismail and Montgomery, 1979). The ability to answer this question is limited by difficulty in equating initial fitness levels and training stimulus magnitude between young and old subjects. Studies with young adults indicate that there is a negative relationship between a subject's initial $\dot{V}O_2max$ and the percent increase with training ($r=-0.54$, Sharkey, 1970). A correlation of -0.63 between the mean values for initial $\dot{V}O_2max$ and percent change in $\dot{V}O_2max$ is obtained from a selection of studies from the literature in which $\dot{V}O_2max$ was directly measured and the average age of the subjects was 55 years or more. This suggests that initial $\dot{V}O_2max$ may be a very important determinant since it explains more than one third of the variation in the training induced change of $\dot{V}O_2max$ despite wide variations in the intensity, duration, and frequency of training among these studies. However, Sidney and Shephard (1978) found no correlation between initial fitness and improvement in cardiorespiratory fitness in their study of elderly subjects. They suggest that this may reflect the small range of fitness levels in the elderly and perhaps poor motivation among the least fit.

Raven and Mitchell (1980) report that with increased age the percent increase attained at a given initial $\dot{V}O_2max$ decreases. However, it may be wrong to equate young and old subjects on the basis of absolute $\dot{V}O_2$. The age related decrease in maximal oxygen uptake

appears to be the same in trained and untrained subjects (Skinner, 1973). In view of this decline an elderly subject with maximum $\dot{V}O_2$ of 40 ml/kg·min is probably physically active whereas a 20 year old with the same $\dot{V}O_2max$ is likely sedentary. Therefore, if young and old are matched on $\dot{V}O_2max$ they will have differing activity levels and conversely if they are matched by activity level the $\dot{V}O_2max$ will differ. If the activity levels are different the same training program will represent a smaller relative increase in stimulus level for the elderly subject and therefore he will exhibit a smaller training response. Shephard (1978), p. 183) suggests that subjects be compared who "are initially at the same percentage of age-related normal standards of maximum oxygen uptake." The problem that arises from this is defining the "normal" standard. Large variations in $\dot{V}O_2max$ are found depending on the test protocol, whether $\dot{V}O_2max$ is directly measured or estimated from submaximal or resting measures, subject nationality and the method of recruiting subjects. Hodgson (1971) reviewed 8 studies where $\dot{V}O_2max$ was directly measured and derived a regression equation ($\dot{V}O_2max$) (ml/kg·min = 6.16-0.44) (age) (years) which predicts a $\dot{V}O_2max$ of 35.2 ml/kg·min for a 60 year old subject. An analysis of a sample of men from the midwestern United States suggested a value of 29.5 ml/kg·min for a sedentary 60 year old and 32.9 for a conditioned sedentary man (Hodgson, 1971). However, even when a correction to precent of an age predicted norm is carried out it appears that the elderly have exhibited smaller gains with training than the young since from Raven and Mitchell's diagram the percent increase for an "average" 25 year old with an initial $\dot{V}O_2max$

of 45 ml/kg·min is approximately 20% versus the 10% gain for an average 60 year old with an initial $\dot{V}O_2$max of 30 ml/kg·min. The average increase from a survey of literature (Hodgson and Buskirk, 1977) was 16.7% for a 30 year old and 11.5 percent at age 60. However, it is probable that the training intensity in these diverse studies was lower for the elderly. The possibility that the negative correlation observed between initial scores and change scores is a statistical artifact has been raised (Williams et al., 1984) but this possibility has not been embraced by exercise physiologists.

Several authors (Badenhop et al., 1983; DeVries, 1971; Hodgson and Buskirk, 1977; Seals et al., 1984; Sidney and Shephard, 1978) have attempted to establish the relation between training intensity and response in the elderly. DeVries (1971) observed a positive relation between exercise training intensity and improvement in fitness (r=0.38). DeVries suggests that an intensity at or above 40% of heart rate reserve is required to produce a change in cardiovascular fitness. The conclusions of this study are weakened by the use of a submaximal test, training with one exercise mode (walk/jog) and testing with another (cycling), and use of age predicted maximum heart rates in determining heart rate reserve. Sidney and Shephard (1978) trained 42 elderly (60 to 83 years old) men and women. After the training records were examined the subjects were divided into four groups on the basis of training intensity and frequency. All subjects except those who trained lightly and infrequently improved their predicted $\dot{V}O_2$max scores (Astrand bike

test) after just seven weeks of walk/jog training. The largest gains were observed in subjects who trained intensely and often. The post-hoc division of the subjects into groups makes it uncertain whether another variable (eg. initial health) might have influenced the results.

A more recent study from Ohio State University (Badenhop, et al., 1983) was more carefully designed and controlled than the two previous investigations. Twenty-eight (7 males, 21 females) university students who were over 60 years of age were randomly assigned to a high or low intensity exercise group. The high intensity group trained at 59.6± 4.3 % and the low intensity group at 38.4± 5.4% of heart reserve. Four subjects served as controls. Approximately the same percent gain in $\dot{V}O_2$max was observed for the high (14.3%) and low intensity (16.8%) groups. There was no significant difference in $\dot{V}O_2$max between the groups at entry or completion of the study. The initial $\dot{V}O_2$max for both groups was low (21.0 ml/kg·min) probably because of the preponderance of women in the sample.

The discrepancy in findings between the studies of Sidney and Shephard (1978) compared to Badenhop (1983) might stem from several sources including the low initial fitness of Badenhop's subjects. Badenhop and his co-authors point out that both the low and high intensity groups were at or above the 40% of heart rate reserve threshold suggested by DeVries. A possible explanation of Sidney's findings is that only high intensity walking or jogging will produce

large gains on a cycle ergometer test. Finally, Sidney and Shephard point out that the Astrand prediction is subject to large systematic errors and has a large coefficient of variation. When studying change scores the measurement error at each test is compounded. The reliability of change scores is notoriously low (Dotson, 1973).

The effect of frequency and intensity of training for 40 men aged 28 to 55 was studied by Oja as reported by Hodgson and Buskirk (1977). Oja found the improvement in $\dot{V}O_2$max was the same for groups who worked at 70 to 80 percent of $\dot{V}O_2$max but that a larger increase in fitness was obtained with 4 sessions per week versus 2 sessions.

The effect of duration of an exercise session or of a training program on cardiorespiratory function has not been systematically explored for elderly subjects. Sidney and Shephard (1978) reported that a smaller (n=22) subset of their subjects continued to train for one year and showed only a small improvement in addition to that observed after 7 weeks of training. DeVries (1970) observed rapid improvement over the first six weeks of training and a slower improvement following that time period. In contrast, Benestad (1965) observed no change in $\dot{V}O_2$max with 5 or 6 weeks of training for a group of very elderly men (mean age 75 yrs). Seals et al. (1984) trained 14 elderly (mean age 63 years) men and women at a light intensity for six months and observed a 12% increase in $\dot{V}O_2$max. A further six months of high intensity training increased $\dot{V}O_2$max by an additional 18%. The range of increase

observed with either training intensity was large (1-42%) and the effects of increased duration and increased intensity are confounded.

Other authors have suggested a mild introduction to exercise for the elderly with a slow increase in intensity over several weeks in order to avoid the high incidence of muscolo-skeletal injuries which has been observed (Shephard, 1978).

In summary, it appears that increased frequency of training will result in more marked improvement in fitness. Increasing training intensity may (Sidney and Shephard, 1978) or may not (Badenhop et al., 1983) produce larger gains. The effect of duration of an exercise session on the training adaptation of elderly subjects has not been studied. The effect of increasing the duration of the program is not clear, however, because of safety considerations, it seems prudent to employ a longer duration program starting with low intensity exercise and increasing the training stimulus level gradually.

2.3.2 Physiological adaptations to training in the elderly.

Despite these complications it is possible to state that the elderly do demonstrate an increase in $\dot{V}O_2max$ as a result of endurance training (Shephard, 1978, p.188). The physiological basis in elderly subjects of this increased maximal oxygen uptake has not been defined. It is not suprising that there is disagreement about the relative contribution of the various components of the cardiorespiratory system to the training response when the variety of training program intensities, modes and durations is considered. In young subjects the relative importance of central and peripheral adaptations is believed to vary with each of the training variables. Additional complications are the wide range of ages subsumed in terms such as elderly and older and the increasing inter-subject variability observed among older subjects (Bafitis et al., 1977).

The effect of training on the pulmonary system is not clear. Niinimaa and Shephard (1978) reported no significant change in pulmonary diffusing capacity, spirometric lung volumes (vital capacity, functional residual capacity, expiratory reserve volume) or closing volume as a result of training. However, the conclusion is weakened by the lack of significant change in $\dot{V}O_2max$ with training since this suggests that the training stimulus applied was not adequate. Reports of increased

vital capacity with training exist (Barry et al., 1966; Chebotarev et al., 1974; DeVries, 1970) but the increases are small. An increase in the maximum minute ventilation following training was observed by several authors Badenhop et al., 1983; Barry et al., 1966; DeVries, 1970; Pollock et al., 1976). It has not been reported whether these gains are due to increased tidal volume or breathing frequency.

There is some disagreement about the effect of training on maximal heart rate. A small decrease in maximum heart rate was observed by some research groups (Niinimaa and Shephard, 1978; Pollock et al., 1976) but not others (Badenhop et al., 1983; Tzankoff et al., 1972). Barry et al. (1966) observed a large increase in peak heart rate with training. However, the initial values recorded were extremely low (peak heart rate 120 bpm, peak $\dot{V}O_2$ less than 17 ml/kg min). There is widespread agreement that heart rate at a given oxygen uptake or worklevel is reduced after training (Badenhop et al., 1983; Barry et al., 1966; Benestad, 1965; DeVries, 1970; Niinimaa and Shephard, 1978; Tzankoff et al., 1972) which is part of the classic training response observed in young adults.

There is very little information about adaptations of the heart in elderly subjects to endurance training. Athletes have larger hearts than their age matched controls (Shephard and Kavanagh, 1978; Heath et al., 1981). While Shephard suggests that " it seems more reasonable to attribute the difference to sustained endurance training" it seems just

as (if not more) reasonable to attribute this cross-sectional difference to self-selection of those who are genetically endowed for competition.

Pollock's group (1976) assessed heart size (chest roentograms), stroke volume and cardiac output (echocardiography) before and after training and found no significant change. Twenty four (18 women, 6 men) normal elderly subjects (mean age 72 yrs.) were studied using radionuclide angiography before and after training (Schocken et al., 1983). Cardiac index at the same workload was increased following 12 weeks of cycle ergometer training. This increase was apparently due to an increased end-diastolic volume with no change in end-systolic volume or left ventricular ejection fraction. The authors suggest that perhaps the failure to observe an improvement in cardiac performance (left ventricular ejection fraction) is because the elderly require longer than 12 weeks to adapt to the training stimulus. They suggest several reasons why no modification of left ventricular performance was observed:

" (1) inability of the heart to respond to the repetitive sympathetic stimulation associated with cardiovascular training, (2) decreased response to augmented pre-load by the Frank-Starling mechanism, (3) inability to respond to exercise-induced increase in afterload, (4) decreased overall contractility rendering specific myocardial training unattainable, (5) inability to improve myocardial oxygen extraction, (6) occult coronary artery disease, and (7) a state of chronic deconditioning in the elderly that is less readily reversed than in

younger persons."

They are unable to discriminate among these possibilities other than by suggesting that their results make both a failure to use the Frank-Starling mechanism and occult cardiovascular disease unlikely explanations. Hartley and his co-investigators (1969) studied the effects of 8 to 10 weeks of endurance training on cardiac output on middle-aged men (range 38-55, mean 47 yrs.). Cardiac output was measured using the dye-dilution technique. Following training maximum cardiac output was increased by 13% and $\dot{V}O_2$max by 14%. Maximum heart rate actually declined slightly and therefore there was a large increase in maximal stroke volume (17%). Stroke volume during submaximal exercise was increased in proportion to the training induced bradycardia. Cardiac output was unaltered at a given $\dot{V}O_2$ or work level. Both before and after training stroke volume followed the same pattern of increase reaching a maximum at 30 to 40 percent of $\dot{V}O_2$max. The 15 subjects studied were selected to exclude those who demonstrated any ECG abnormalities at rest or during exercise.

The data from Schocken's study suggests that short term exercise training does not improve cardiac function while the information from Hartley's group suggests that much of the increase in $\dot{V}O_2$max is due to increased cardiac output. The difference may arise because of the 25 year discrepancy in age, or because of the difference in what measures were made. Unfortunately, there is little information available to help resolve the problem. The data from submaximal measures of cardiac output

is no more consistent than the maximal measures. Niinimaa and Shephard (1978b) found a slight drop in cardiac output at a given $\dot{V}O_2$ after training. This decrease was due to a fall in heart rate and unchanged stroke volume. DeVries (1970), employing the CO_2 rebreathing method, observed no change in cardiac output, stroke volume or peripheral resistance at a 75 Watt workload with training. Seals and his colleagues (1984) observed a small rise in stroke volume at the same absolute $\dot{V}O_2$ with indirect Fick (CO_2) determination of cardiac output. These authors attributed most of the rise in $\dot{V}O_2$max with training to an increase in maximal a-$\bar{v}O_2$ difference.

The effect of training on arterio-venous oxygen content difference is simply a reflection of the changes in cardiac output since the difference is calculated from the oxygen uptake and cardiac output measures. No direct measures of the difference across the working muscle in the elderly have been made. Niinimaa and Shephard (1978) found that a-$\bar{v}$ O_2 content differences in the elderly at a given workload were higher than that observed in young subjects. Niinimaa and Shephard (1978) have speculated that training effects on systemic arterio-venous oxygen content differences in the elderly are unlikely because a change in muscle capillarization in the elderly cannot be brought about by training and while changes in muscle enzyme activities may increase oxygen extraction this will be offset by redistribution of flow to the non-exercising tissue.

In summary, it appears that there is no clear understanding of how training induced increases in maximal oxygen uptake are obtained in the elderly. Reports of increases in maximum ventilation (Badenhip et al., 1983), maximum cardiac output (Hartley et al, 1969), maximum systolic blood pressure (Barry et al., 1966), maximum $a-\bar{v}O_2$ difference (Seals et al., 1984), and aerobic enzyme levels (Suominen et al, 1977) exist. However, studies which found no change in each of these variables also exist. The resolution of these discrepancies lies in research which is directed at the physiological mechanisms underlying the response to physical training rather than simply whether they are able to adapt to a training stimulus.

CHAPTER THREE

GENERAL METHODS

3.0 Introduction

The methods and procedures which are common to several of the studies in the following chapter are described in this section. These methods include the process for recruiting subjects, and the anthropometric and physiological measurements used to characterize the subjects. In addition, the exercise tests used to evaluate the gas transport system are outlined. Description of the data management system and the statistical analyses are also included.

3.1 Subjects

Two hundred and twenty four subjects were recruited over a 3 year time span. Company personnel offices were contacted to arrange presentations to employees who were about to retire. Newspaper advertisements were also placed to reach those who were not employed with a large firm and brochures describing the program were distributed. In the later years men who were already in the program often encouraged friends and acquaintances to participate.

All subjects were fully informed of the risks and discomfort involved with each procedure and were advised that they could be assigned on a random basis to either the activity or control group. Written consent was obtained from each subject before any tests were performed (See Appendix B).

The criteria for acceptance into the study included: 1) chronological age between 55 and 67 years at entry; 2) able to walk at 80 m/min on a motor driven treadmill; 3) available for initial testing at least one month before retirement. An additional 6 subjects were employed in an "advisory" role. These subjects had retired before the study was initiated and therefore could not be included in the analysis. However, they underwent the full test battery and participated in the training program. This allowed refinement of the testing and training methods without degrading the quality of the data by altering methodology after data collection had started.

A medical history and physical examination, including a 12 lead EKG tracing at rest, were obtained. A sample of venous blood was sampled from the fasting subject. Cholestorol, high density lipoprotein, and triglyceride levels were assessed as were haematocrit and haemoglobin levels.

Skinfold thicknesses were measured on the right side of the body using Harpenden calipers at the following sites; chest, tricep, bicep, subscapular, umbilical, suprailiac, thigh and calf. Skinfold data is presented as the sum of thicknesses at the eight measurement sites. Pulmonary function was measured using an eight liter wet seal spirometer (Collins). Vital capacity (VC), forced expiratory volume in one second (FEV1.0), and maximum mid-expiratory flow rate (MMEFR) were recorded from the highest of three trials.

Activity over the year previous to entering the study was assessed using the Minnesota Leisure Time Activity questionnaire (Taylor et al., 1978). An activity metabolic index score (AMI) was calculated for low, medium and heavy intensity activities. Heavy intensity activities were defined, for the purpose of these studies, as those which required energy expenditures greater than 5.0 times the resting metabolic rate. This demarcation point was selected to approximate 60% of an elderly male's $\dot{V}O_2max$.

3.2 Study Design.

Subjects were randomly assigned in blocks of ten subjects to the control or activity group. Stratification by blue or white collar job classification was performed. All subjects underwent testing at entry to the study and approximately 6 and 12 months later. Variations of up to one month from the 6 or 12 month anniversary date were permitted.

3.3 Exercise Tests.

The data were collected in an air conditioned laboratory with temperatures of 19 to 23.5°C and humidity of 25 to 67%. Simultaneous on line computer collection and ink jet recording on paper were employed for data collection. Subjects were habituated to treadmill walking on their first exposure to the laboratory and underwent maximal tests on their second and third visits. Gas exchange was calculated using the open circuit method. The volume of air inspired was measured using a dry-gas meter (Parkinson-Cowan); samples of mixed expired gas were withdrawn from an 8 liter mixing box and the fractional concentrations of oxygen (fuel cell analyzer) and carbon dioxide (infrared analyzer) were determined. A low resistance Y valve (Lenox and Koegel, 1974) valve was used to separate inspired and expired gas flows. Heart rate was read from a continuous electrocardiographic tracing from a modified CM5 lead.

All subjects were habituated to treadmill walking on their first visit to the laboratory. Alterations in grade and speed were made to familiarize the subject with the sensations and sounds associated with varying speeds and inclines on the treadmill. Subjects were instructed to abstain from caffeine and smoking 2 hours before and to avoid strenuous activity 24 hours before all stress tests.

Subjects who employed drugs that influenced cardiorespiratory function were tested after stopping their medication. This was necessary to ensure that differing levels of medication or a change in drug status did not influence our measurement of their exercise capacity. Another test for setting the exercise prescription was completed with the subject using his medication. This was particularly important for subjects who employed a β-blocking drug whose heart rate response to exercise while on the drug was minimal. (See Appendix C).

During the second session a Stage I (Jones and Campbell, 1982) incremental test to a voluntary or symptom limited maximum was performed. The protocol for this test was 4 minutes of walking at 80 m.min-1 on the level, followed by grade increases of 2.5% every two minutes until the test was halted or a 20% grade was achieved. Following two minutes of walking at a 20% grade the speed of walking was increased by 8 m.min-1 every two minutes until a maximum was encountered.

At least 24 hours intervened before the third laboratory visit. During this session a Stage II test was performed by the first one hundred and forty five subjects. The protocol for the Stage II test includes exercising at three submaximal loads which were selected to elicit heart rates which were 50, 60, and 70 % of the difference between the resting and maximum heart rates. Exercise at each of these loads was continued for 5 to 6 minutes until a cardiovascular steady state was achieved. This was defined as a change in heart rate of less than 5 beats per minute between minutes 3.5 to 4.5 or 4.5 to 5.5. When steady state conditions were achieved respiratory gas was collected for one minute. This was immediately followed by a CO_2 rebreathing manuever. There was a 4 to 7 minute rest before exercise at the next level was initiated. Following the third rest period an incremental test to maximum beginning at a work level at or slightly above that used in the third submaximal steady state load was begun. Other than starting at approximately 80% of $\dot{V}O_2$max the protocol was identical to that used in the Stage I test. Two test protocols were followed in the second test for the remaining subjects. Those subjects who completed one minute at a 15% grade were tested using a modified version of the Stage I in which workload increments were doubled to 5% grade increments and 16 m.min-1 speed increments. Subjects (n=24), who were unable to exercise beyond a 12.5% grade on their initial Stage I repeated the same test protocol on their second test.

The end point of each test was recorded whether the subject called a halt or the supervising physician stopped the test due to one of the changes listed below. Further details are given in Appendix C.

1. Fatigue (subject halted test)
2. ST segment depression
3. Angina
4. Electrocardiographic arrhythmias
5. Claudication
6. Syncope
7. Second or third degree heart block
8. Fall in systolic blood pressure (10-20 mmHg)
9. Rise in systolic pressure above 240 mmHg
10. Other

3.4 Training Program.

Medical supervised training sessions were offered three mornings a week. Subjects were encouraged to train one additional time each week. Training intensity was based on the results of the initial Stage I test. The following formula was used to calculate the training heart rate; Training heart rate (bpm) = ([60maxMets]/100(Maximum heart rate-resting heart rate) + resting heart rate (Cunningham et al, 1974). This exercise prescription was revised for all subjects on the basis of another Stage I test carried out 6 months following the initial test. If

rapid progress was evident after 3 or 9 months an additional test was performed to allow updating of the exercise prescription. Subjects were assigned to exercise leaders in groups of 10 to 15. Exercise leaders taught the men to palpate their heart rate (Pollock et al., 1972) and initially accompanied them while walking or jogging to teach pacing. Subjects were encouraged to start slowly and work toward matching their target heart rate over the first 3 to 4 weeks of training. Exercise sessions were held outdoors during moderate weather on a 400m track with an artificial surface and on a 200m indoor track when conditions were inclement. Each training session consisted of a 10 to 15 minute warm-up, approximately 30 minutes of walking or jogging at a pace set to elicit the prescribed heart rate, and a 10 minute warm-down. The subjects recorded distance travelled, time spent walking or jogging and the pre-, mid- and immediately post-exercise heart rates for both supervised sessions and any additional training which they undertook. During the supervised sessions exercise leaders frequently checked pulse rates to ensure accuracy in recording the heart rate values.

3.5 Data Analysis and Statistical Methods.

Data were initially recorded on forms before being entered into a general data base on the departmental computer. This data base and the accompanying software permitted data checking for missing values and out of range values. Rudimentary data analysis such as means and standard deviations within groups or for a subgroup of subjects who met a criterion value on another variable were performed on the departmental computer. Further data analysis required transfer of the information to the Natural Science Computing Centre. The Statistical Package for the Social Sciences (SPSS) (Nie et al., 1975) was used for further data manipulation and statistical analysis.

Several of the analyses in this thesis employ the simple (bivariate) or multiple (multivariate) regression techniques. The purposes of regression analysis are two-fold: 1) to describe the strength and direction of the relationships among variables and 2) to test hypotheses.

A brief review of simple bivariate regression will introduce the principles underlying regression analyses which can then be extended to the multivariate situation. In bivariate regression the values of a dependent variable (Y) are predicted from an independent variable (X) using the linear equation.

$Y' = A + BX$

where Y′ represents "the estimated value of the dependent variable Y, B is a constant by which all values of the independent variable X are multiplied, and A is a constant which is added to each case" (Nie et al., 1975, p. 323). B is the "slope of the regression line and indicates the expected change in Y with a change of one unit in X" (Nie et al., 1975, p 323). Generally, the estimated values of the dependent variable (Y′) will not equal the actual values (Y). The difference between them (Y-Y′) is termed the residual. In least squares regression the values of A and B are selected to minimize the sum of the squared residuals ($(Y-Y')^2$). The total variance in the dependent variable (sum of squares of Y, SS_y) can be separated into two components 1) the variance explained by knowledge of the independent variable and application of the regression equation (SS_{reg}) and 2) the residual or unexplained variance (SS_{res}). The ratio of explained variance to total variance is referred to as the coefficient of determination ($r^2_{xy} = SS_{reg}/SS_y$) and represents the proportion of variation in Y explained by the regression equation. The square root of this quantity (r) is the more familiar Pearson product-moment correlation coefficient which describes the "goodness of fit" of the regression equation to the actual data values (Nie et al., 1975, p. 324).

The relationship between a dependent variable and one independent variable may be confounded by interactions between the explanatory variable of interest and other independent variables. Multiple

regression allows the researcher to evaluate the effect of each independent variable while controlling for variation in the other variables. The multiple regression technique also allows quantification of the total amount of variation in a dependent variable explained by a set of independent variables. In multiple regression the general form of the equation is

$$Y = A + B_1X_1 + B_2X_2 + \ldots B_iX_i,$$

as in simple regression Y is the predicted value of Y, A is the Y intercept, and B_1 and B_i are the regression coefficients. Again the values of A and the B's are selected to minimize the sum of squared residuals ($(Y-Y')^2$). The B's which are computed are actually partial regression coefficients since the Bi expresses the relation between Xi and Y while the effect of the other independent variables is held constant. The square of the multiple regression coefficient ($R^2 = SS_{reg}/SS_y$) is a summary measure which expresses the amount of variation in Y which can be predicted from knowledge of all the measured independent variables and is analogous to the coefficient of determination (r^2) of simple regression.

In stepwise regression, which is the multiple regression variant used in this thesis, the independent variables are incorporated into the equation in descending order, ranked by the amount of variance explained.

Two statistical tests can be made in the regression analysis; 1) the overall goodness of fit of the regression equation (r, R) and 2) in multiple regression the contribution of an individual independent variable after the effect of all other independent variables is controlled can be evaluated.

The regression coefficient B may be standardized in a manner analogous to the Z_c transform used in performing Student's t-tests. The B is standardized by multiplying by the ratio of the standard deviation of X over the standard deviation of Y (sd X/sd Y). The standardized coefficient (β) is especially useful in comparing regression coefficients between variables which are measured on different scales. The F ratio

$$SS_{reg}/(SS_{res}/[N-2]),$$

can be used to test the null hypothesis that the degree of association indicated by the standardized coefficient β could arise due to chance. The F ratio is evaluated in the usual manner by comparision with a table of critical values. The same transform to standardize the B's can be performed in multiple regression and the significance of the partial regression coefficient can be evaluated. This allows us to test whether each independent variable explains a statistically significant amount of variation in the dependent variable.

Categorical variables can be included in a multiple regression. This type of analysis is employed to test the research hypothesis that the two groups, represented by the categories, are different after the effect of the other independent variables is held constant and is computationally equivalent to a multivariate analysis of variance in the two group case (Donner and Cunningham, 1983). This technique is used in this thesis to test whether differences between the control and activity groups are statistically significant.

CHAPTER FOUR

THE PAPERS

4.1 Measurement of Maximum $\dot{V}O_2$ in the Elderly

Introduction.

The first task in defining what physiological factors determine aerobic capacity is to find a measure that is a reliable indicator of aerobic capacity in the elderly. Maximum oxygen uptake measured in young subjects is reliable and reproducible when the criteria of a plateau in oxygen consumption, adequate exercising muscle mass, and appropriate test duration (5 to 15 minutes) are employed. Maximum oxygen uptake is regarded as the best measure of aerobic capacity (Rowell, 1974) and is used to describe the fitness of a group and to quantify the effects of various training regimes. Objective evaluation of the functional limits of the gas transport system in the elderly may be complicated by difficulty in insuring that the subjects exercise to fatigue and thereby attain a plateau in oxygen consumption. This problem may be further complicated by the presence of respiratory or cardiovascular disease in many older subjects (Taylor and Montoye, 1972; White, 1950).

Interpretation and comparison among training studies is difficult because investigators have reported bradycardia at a given $\dot{V}O_2$, increases in $\dot{V}O_2$ at a set heart rate and estimated or symptom limited maximum oxygen uptakes derived from various test protocols. Precise quantification of cardiorespiratory fitness with a reproducible (difference between repeated measures) and reliable (correlation between repeated measures) measure is required if the efficacy of various training regimes is to be assessed (Dotson,1973). The reliability of maximum uptake values in the elderly has received little attention (Sidney and Shephard, 1977). Investigators have reported that the elderly have varying success in meeting the plateau criteria for maximal oxygen consumption (Astrand et al., 1959; Sidney and Shephard, 1977).

The reliability and reproducibility of maximum oxygen uptake measures were evaluated in a large sample of elderly men (55 to 68 years of age). The effect of test protocol and test repetition on the maxima achieved and on the proportion of subjects exhibiting a plateau in maximum oxygen uptake was observed. Furthermore, we examined the proportion of elderly men who stopped a maximal exercise test because of volitional fatigue or whose test was halted due to angina, ECG abnormalities, a fall in systolic blood pressure, or claudication. The agreement between a submaximal (increase in oxygen uptake at a given heart rate) and a maximal ($\dot{V}O_2$max) measure of training was studied.

Methods.

The subjects were recruited as described in the general methods section (3.1, Table 1). The subjects were informed of procedures and the attendant risks and discomfort before giving their consent to participate.

Test Protocol.

A 12-lead ECG was obtained from each subject before exercise testing and the subjects were familiarized with the laboratory and treadmill walking on their first visit. An continuous treadmill test in which grade increments of 2.5% were made every other minute (Stage I) (see Chapter 3.3 for details of test protocol) was completed in the second laboratory session. On the third visit one of the following tests was carried out; a repeat of the Stage I test, a Stage II test, or a modified Stage I. The Stage II test involved three submaximal loads separated by 3 to 4 minute rests and then a continuous progression to $\dot{V}O_2$max in 2.5% grade increments from approximately 70% of $\dot{V}O_2$max. The modified Stage I test consisted of the same pattern of change as the Stage I but with increases of 5% grade. The interval between second and third visits ranged from 48 hours to one week. The first 145 men underwent the Stage I and Stage II tests (Group I-II). The remainder of the sample were assigned to a repeat Stage I test (Group Repeat I) if they reached a 15% grade or less on the initial Stage I test and to the modified Stage I (increment in grade or speed doubled)(Group Mod. I) if they attained more than a 15% grade. The split between a repeated Stage I and a

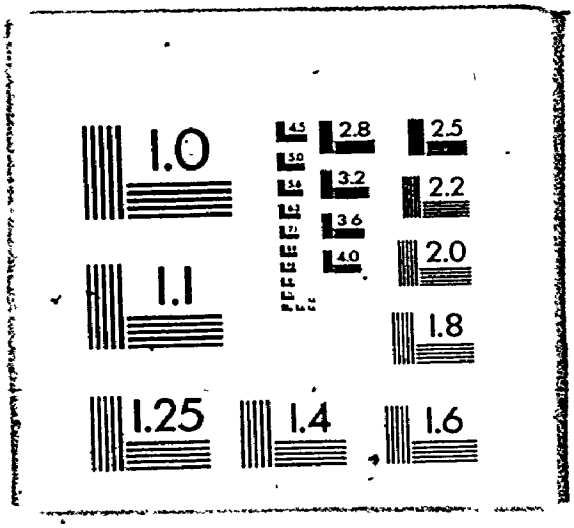
Table 1. Physical characteristics of the subjects who underwent each test type. Values are means (range).

Group	Age(yrs)	Weight(kg)	Height(cm)
All Subjects (n = 224)	62.3 (55-68)	79.3 (53.0-111.3)	173.8 (152.9-196.4)
Repeat I (n = 24)	61.7 (55-67)	82.6 (53.0-104.6)	175.6 (164.8-186.8)
Stage I-II (n = 145)	62.3 (55-68)	79.5 (59.6-111.3)	173.6 (152.9-196.4)
Mod. I (n=38)	62.2 (55-65)	78.7 (60.9-99.6)	175.2 (161.9-189.4)

modified Stage I test was done to equalize the test duration between the fit and unfit subjects. Increased test duration may decrease the observed maximum $\dot{V}O_2$. $\dot{V}O_2max$ is significantly higher in the group (fit) that did a modified Stage I test compared to those subjects (unit who repeated the Stage 1 test. The description of the subject in each group is found in Table 1.

The reason for stopping the test was recorded and used in subsequent analyses to separate symptom limited efforts from those curtailed by fatigue. All subjects were tested 48 hours after halting any medications that influence cardiorespiratory function (e.g., β-blockers, antiarrhythmics) to ensure that drug dosage did not influence the test end point.

One half of the subject sample was randomly assigned to a one year training program which involved walking or jogging at a prescribed heart rate. Sessions were held three times per week. Exercise sessions are described more fully in the general methods section (3.4) and in Chapter 4.4. Only results from those who completed the full year of training are utilized in this paper. The response to submaximal exercise after training was assessed by calculating the change from initial to final testing in $\dot{V}O_2$ at a fixed heart rate (125 bpm). This change was compared with the change in $\dot{V}O_2max$ to assess the relation between a submaximal and a maximal measure of the training response.


1.0
1.1
1.25
1.4
1.6
2.8
3.2
3.6
4.0
2.5
2.2
2.0
1.8

Analyses of Data.

A plateau in oxygen consumption was defined as an increase less than or equal to 2 ml per kilogram of body weight per minute with a change in worklevel (grade or speed) (Taylor et al., 1955). Comparisions between symptom and fatigue limited tests of maximal values for oxygen uptake, respiratory exchange ratio, heart rate ventilation and the proportion of subjects reaching a plateau in oxygen consumption were made. The same measures were also compared between groups; Repeat Stage I, Stage I-II, Mod. Stage I. Statistical evaluation of differences was done by using the paired or unpaired t-test. The correlation among measures was assessed using the Pearson product-moment correlation coefficients (Nie et al., 1975).

Results.

In the first maximal treadmill test 33.6% of the complete sample (n=224) of these elderly men reached a plateau in oxygen consumption (Table 2). Twelve percent (27 subjects) of the tests were halted by the physician because of symptomatic changes and nine of these subjects also exhibited a plateau in oxygen consumption. When all subjects with a symptomatic limit are removed from the analysis the proportion of men reaching a plateau rises to 34.4%, $\dot{V}O_2$max increases 3%, and the maximum heart rate increases from 155 to 158 bpm for the group as a whole. The $\dot{V}O_2$max was not significantly different between

Table 2. Maximal oxygen uptake of subjects in each group attaining a plateau in oxygen consumption compared to those not reaching a plateau. Effect on proportion plateauing of removing subjects with symptom limited maxima.

Group	Test Type	% Reaching a Plateau		Maximal Oxygen Uptake[b] (ml/kg/min)	
		Total	Fatigue[a]	Plateau	Non-plateau
All Subjects (n=224)	Stage I	33.6	34.4	28.3	29.1
Repeat Stage I (n=24)	Stage I(1)	33.3	36.4	23.0	25.5
	Stage I(2)	45.8[c]	47.4[c]	26.0	25.9
Stage I-II (n=145)	Stage I	35.2	36.4	27.6	28.4
	Stage II	31.0	32.2	28.5	29.3
Modified Stage I (n=38)	Stage I	34.2	42.1	32.1	31.4
	Mod. I	42.1[c]	43.2	31.0	32.5

[a] Fatigue indicated that only subjects reaching subjective fatigue and not those whose test was stopped for medical reasons are included.

[b] $\dot{V}O_2$max for all subjects, fatigue and symptom limited.

[c] Proportion of subjects who reached a plateau in $\dot{V}O_2$ increased significantly from the first to second test ($p<0.05$).

those exhibiting a leveling off of $\dot{V}O_2$ (28.1 ml.kg-1.min-1) and those subjects who did not reach a plateau (28.4 ml/kg min). Data was not available for a second initial test of 17 subjects. A significantly increased proportion of subjects did demonstrate a plateau when the same or a similar test was repeated (Table 2). A second discontinuous test (Stage II) did not increase the numbers who fulfilled a plateau criteria. The percent of subjects reaching a plateau increases for the Modified Stage I group when those men with a symptomatic limit to their test are eliminated from the analysis. This was not observed for the subjects who second test was a repeat of the Stage I or a Stage II.

Paired differences between the first and second maximum tests were compared for each of the Groups (Table 3). The maximum $\dot{V}O_2$ reached on the second test was significantly higher for the groups which repeated a Stage I test (5.07%), or followed the stage II test protocol (3.45%), but not for the Modified Stage I group (0.76%). Although, there was a significant difference between the $\dot{V}O_2$ max reached on the initial Stage I test and all second tests regardless of test protocol (1.2 ml/kg min, 4.2%) the magnitude of change is below the criteria for a plateau. The second test resulted in a higher $\dot{V}O_2$ for 56.3% of the subjects. Scattergrams illustrating the relationship between the maximum attained on Stage I and each of the tests are shown in Figure 3,4,5. The correlation between the first and second tests for $\dot{V}O_2$ max was high for the repeated Stage I test (0.90) and moderately high between the Stage I and II tests (0.87) and modified Stage I group (0.67).

Table 3. Comparison at entry between first and second treadmill test of maximum values of oxygen consumption, ventilation, and heart rate for each group. Groups as in Table 2. (Means ± S.E.).

	Repeat Group (n=24)		Group I-II (n=145)		Modified Group (n=38)	
	Stage I(1)	Stage I(2)	Stage I	Stage II	Stage I	Mod. Stage I
$\dot{V}O_2$ max (ml/kg.min)	24.7±1.1	25.9±1.3	28.1±0.5	29.1±0.4	31.7±0.8	31.9±0.8
Mean Difference	1.25*		0.97*		0.24	
Correlation (r)	0.90		0.87		0.67	
$\dot{V}_E$ Max. (l/min)	64.9±3.4	68.5±4.1	75.6±1.7	81.1±1.8	84.1±2.9	83.2±2.6
Mean Difference	3.6		5.5*		0.9	
Correlation (r)	0.87		0.81		0.70	
Heart Rate Max. (b/min)	146±4	149±3	152±2	157±1	161±2	159±2
Mean Difference	3		5*		3	
Correlation (r)	0.78		0.83		0.81	

* Difference between test protocols is significant at $p < 0.05$.

The correlation between tests on which a plateau was achieved is higher than that observed for non-plateau tests when any of the second tests is compared with the first Stage I except for those cases where the second test was a repeat of the Stage I (Table 4).

The changes in $\dot{V}O_2max$ for the subgroup that undertook endurance training are tabulated by test type (Table 5). The change in $\dot{V}O_2max$ from initial to final testing was larger for those members of the training group whose second test at both entry and completion of the study was a repeat of the Stage I test (Table 4). However, the increase (31.2%) observed with the 7 subjects who performed a repeat of the Stage I test before and after training was not larger than that observed for them when the comparison from initial to final testing is made on the first Stage I (1) test (31.2%). This large increase represents a difference in subject response rather than a difference in test asssesment (Table 5) and may be due to their lower initial fitness level (Pollock, 1973). The increase in $\dot{V}O_2max$ as a result of training was significant for each subgroup and test type. There was no significant change in $\dot{V}O_2max$ for the control group. The correlation for the control group between $\dot{V}O_2max$ measures made at entry versus 6 months later, and entry versus 12 months later using the Stage I test were 0.81 and 0.77 respectively. The relation between change in $\dot{V}O_2max$ with training as measured by Stage I and change measured by the Stage II tests is illustrated in Figure 6.

Table 4. Comparison of correlation coefficients between the first Stage I and the second test (repeat of Stage I, Stage II, or modified Stage I protocol) for all tests and for tests where a plateau was reached or not.

First Test Type	Second Test Type		
	Repeat Stage I	Stage II	Mod. Stage I
All Stage I	0.90 (24)*	0.87 (145)	0.67 (38)
Plateau on Stage I	0.67 (8)	0.92 (50)	0.86 (13)
Non-plateau Stage I	0.96 (16)	0.83 (95)	0.60 (25)

Values are Pearson Product Moment Correlations, all are significantly different from zero.

* Number of subjects tested.

Table 5. Comparison among measures of training induced change in $\dot{V}O_2$max for those subjects who completed the specified test protocol at both entry and at completion of the training program.

Test	$\dot{V}O_2$max (ml/kg/min)		Mean difference	
	Initial Test	Final Test	ml/kg/min	%
Stage I (n=88)	29.1	33.0	3.9	13.3
Stage II (n=48)	29.7	33.5	3.9	13.1
Modified Stage I (n=16)	33.4	36.6	3.2	9.5
Repeat of Stage I (n=7)	24.0	31.5	7.5	31.2
Best Maximum (n=88)	30.8	34.5	3.7	12.1

Note: All subjects did an initial Stage I test (n-88). A second maximal test (repeat of Stage I, Stage II, or modified Stage I) was then completed. The best maximum values are obtained by selecting the highest $\dot{V}O_2$ regardless of test protocol. Differences between initial and final $\dot{V}O_2$ values are significant for all test protocols.

Figure 3. Scatterplot illustrating the relationship between $\dot{V}O_2max$ (ml/kg/min) obtained from a Stage I protocol and the $\dot{V}O_2max$ for that subject obtained from a repeat Stage I protocol treadmill test. The line of identity is plotted. Simple correlation coefficient (r) is 0.90. (n=24).

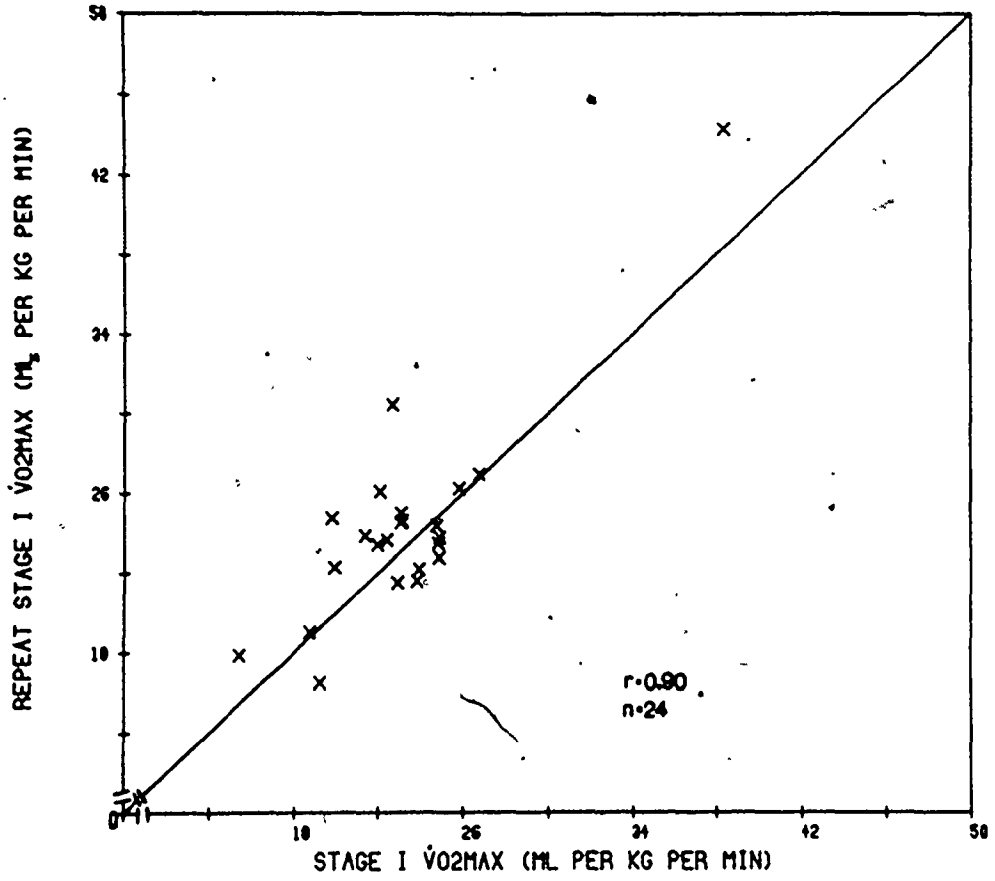


Figure 4. Scatterplot illustrating the relationship between $\dot{V}O_2max$ (ml/kg·min) obtained from a treadmill test which followed a Stage I protocol and the $\dot{V}O_2max$ for that subject obtained during a Stage II protocol treadmill test. The line of identity is plotted. Simple correlation coefficient (r) is 0.87. (n=145).

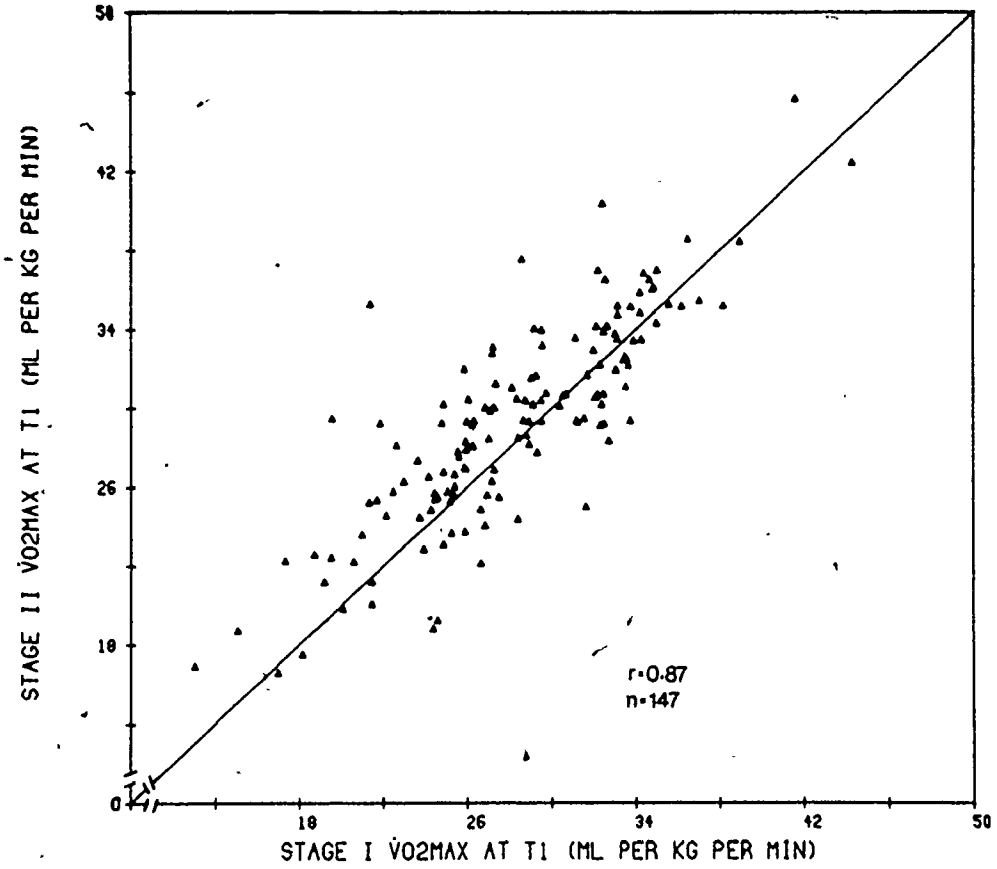
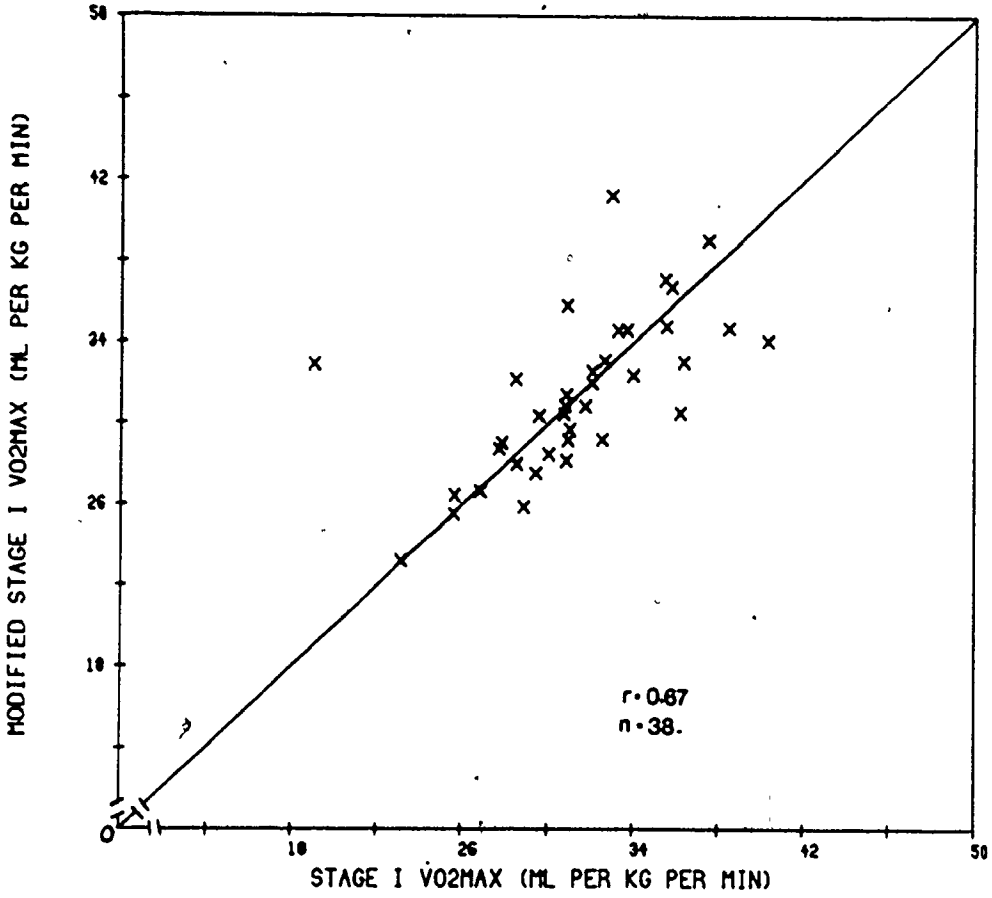


Figure 5. Scatterplot illustrating the relationship between $\dot{V}O_2max$ (ml/kg·min) obtained from a Stage I test and the corresponding value obtained from a modified Stage I protocol test. (r=0.67) (n=38).



The correlations between change as measured by the first Stage I test, the repeat Stage I(2) (r=0.88) and the Stage II (r=0.73) and the modified Stage I (r=0.71) are significant and moderately strong.

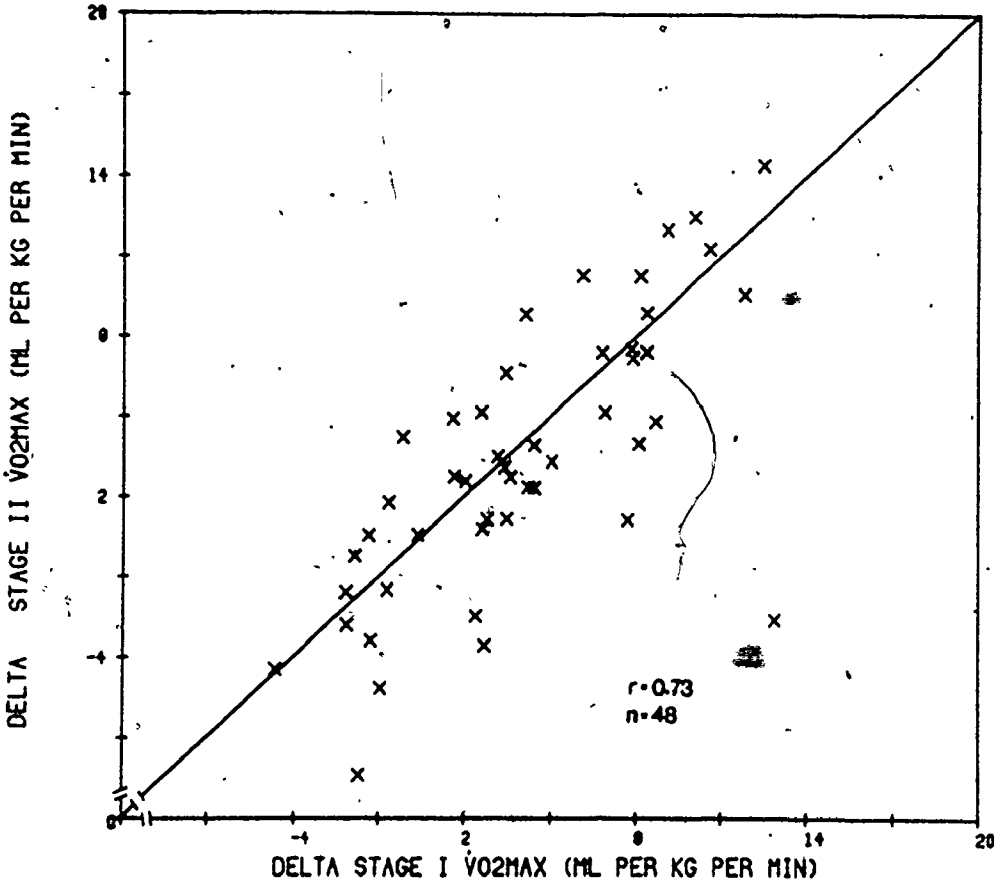
The oxygen uptake at a common heart rate (125 bpm) was obtained for each subject in the training group, by interpolation from the first Stage I test. Extrapolation of up to 5 beats was done when necessary (4/88 tests). Those subjects who did not reach a heart rate of 120 bpm were eliminated from the analysis (n=3). The increase in $\dot{V}O_2$ at a given heart rate from initial to post-training testing was calculated. The increase in $\dot{V}O_2$ at heart rate equal to 125 bpm was compared with the change in $\dot{V}O_2$max on the Stage I test and the change in $\dot{V}O_2$max with training for the highest $\dot{V}O_2$max regardless of which test type it occurred on. The correlation between the maximal and sub-maximal measures of training response is significant but the simple correlation is only 0.64 ($p<0.05$).

Discussion.

The major finding of this study was that the reliability of the maximum oxygen uptake measure in the elderly is acceptably high despite our finding that only approximately one third of our men demonstrated a plateau in oxygen consumption. The small proportion reaching a plateau in uptake was not due to test curtailment as a result of symptomatic changes since the proportion of plateaus achieved rose only slightly

when symptom limited tests were removed from the analysis. The difference between first and second measures of $\dot{V}O_2$max at baseline was statistically significant but within the range of intra-individual variability. Our ability to assess training induced change in $\dot{V}O_2$max is adequate for direct maximal measures. The average maximum uptake achieved in the sample compares favourably with those reported in other studies with the elderly (Seals et al., 1984; Shephard, 1978, p 106; Sidney and Shephard, 1977; Taylor and Montoye, 1972). The number of subjects reaching a plateau did rise slighty with repetition of the same or a similar test protocol. However, use of a discontinous protocol in the second test did not increase the fraction achieving a plateau. Sidney and Shephard (1977) found a higher fraction (69%) of their subjects reached a plateau. A possible explanation for this lies in their medical screening which eliminated 21% of their subjects and in subject self selection to participate in an exercise training program. Although our subjects underwent a medical examination no subjects were eliminated on the basis of the results of that examination. The subjects were aware that they could be randomly assigned to either a control or activity group. The average maximum uptakes for the male subjects in Sidney and Shephard's study was 30.2 ml/kg/min versus an average value of 29.3 on the second tests in this study. The initial $\dot{V}O_2$max averaged 31 ml/kg/min for 22 men (age range 49-65, mean age 55 yrs) who volunteered for an endurance training program (Pollock et al., 1976). A plateau in oxygen consumption was manifested by 73% of these subjects. The treadmill test protocol employed by Pollock and his co-workers is

Figure 6. The relationship between change in $\dot{V}O_2max$ from before to after training measured using tests following a Stage I protocol versus the training induced change measured using a Stage II test is illustrated using a scatterplot. The line of identity is plotted. The least squares regression equation for the relation is (Change in $\dot{V}O_2max$ on Stage II = 0.97[Change in $\dot{V}O_2max$ on Stage I] - 0.03 (ml/kg/min), r=0.73)



very similiar to the Stage I protocol used in this study. Katch and co-workers (1982) observed plateaus in 61% of 80 tests carried out with 5 young subjects. The reliability of maximum oxygen uptake measures in the elderly has seldom (Sidney and Shephard, 1977) been reported on. Despite the reduced proportion of subjects reaching a plateau it appears from our results (Table 3) that the reliability is approximately the same for the elderly as that observed for young adults (Mitchell et al., 1958; Rowell, 1974). The reliability is generally higher if a plateau is achieved. The low reliability between the Stage I test and repeat test may reflect the small sample size in this group. The percent of young boys (Cunningham et al., 1977) reaching a plateau is also reduced with respect to young adults. A possible explanation for both groups is that their low capacity for anaerobic exercise limits the ability to sustain exercise at $\dot{V}O_2$max long enough to demonstrate a plateau (Cumming and Borysyk, 1972). The physiological mechanism which limits exercise performance in the elderly may also influence the probability of observing a plateau in oxygen consumption. For example, if increasing respiratory muscle oxygen uptake limits exercise a plateau in oxygen consumption may not be observed despite the subject encountering a physiological rather than a motivational limit to exercise. The reproducibility of the test is approximately the same for those in which a plateau was not reached as for those in which a plateau was observed.

Test repetition in this study resulted in a significantly higher maximum for the group as a whole although only slightly better than half

of the subjects demonstrated an increase on the second test. The magnitude of the mean difference between repeated tests is small (approximately 3%) but inspection of the scattergrams indicates that the error in an individual determination may be large. Two and possibly three maximal tests are required to characterize the cardiorespiratory capacity of an individual elderly subject. The variance in $\dot{V}O_2$max with repeated measures on young adult subjects in 5.6% (Katch et al., 1982). This variance is a combination of biological variability and measurement error. Katch points out that because of this large variability a control group is required to seperate training effects from differences due to biological variation. In studies of the group training responses of the elderly repeated initial and final testing or use of a control group is required to assess the effects of training rather than training plus test habituation.

The three test types used in this study allow us to make the following observations and recommendations. First, for most elderly subjects a second maximal test elicits a higher uptake and therefore should be used if precise quantification of cardiorespiratory capacity is required or if a control group is not employed. The choice of protocol depends on the purposes of the investigator. The Stage II test has the advantage of allowing characterization of the steady state responses of subjects and performance of additional measures such as cardiac output determination. Modification of the Stage I test protocol to shorten test duration did not result in an increase in maximum $\dot{V}O_2$

and has the disadvantage of decreasing the number of submaximal data points available for determination of such measures as the ventilation threshold. Davis and his colleagues (1983) found that prolonging a test in which workload increased in a smooth ramp pattern resulted in lower $\dot{V}O_2$max values. If data concerning submaximal steady state conditions is not required it appears that a repeat of the Stage I test may be the most appropriate choice. Since the object of the $\dot{V}O_2$max measure is to characterize the maximum ability to utilize oxygen it is appropriate that the highest maximum uptake achieved should be reported in describing the subject regardless of which test it occurred on.

The ability to accurately assess training induced changes is required before the efficacy of exercise can be determined. A variety of responses to exercise training by the elderly has been described and a portion of this variation may be due to differing methods for assessing the training response. Prediction of maximum $\dot{V}O_2$ by extrapolation to an age predicted maximum heart rate from submaximal data has been critized because of the wide range of maximum heart rates observed for the elderly and because of systematic underprediction of $\dot{V}O_2$max (Sidney and Shephard, 1977). Alternate methods of describing the training response have included physical work capacity at a specified heart rate (PWC150 or PWC130) and heart rate at a given oxygen uptake (Davies, 1972). These measures have been utilized for two reasons. The first is reluctance on the part of the investigator to subject and older person to a maximal test procedure. In a total of approximately 1300

tests on men between 55 and 68 years of age, including those with previous myocardial infarctions and coronary heart disease, we experienced no emergencies. Shephard (1978, p. 88) reported on previous work which suggests that a rate of 1 in 10,000 for incidents requiring emergency action is typical. It has not been established how much use of a maximal versus submaximal test increases the risk of infarction or other emergencies. The second reason for avoiding maximal tests has been uncertainty about the reliablity of $\dot{V}O_2$max measures in the elderly. Our results suggest that two continous maximal treadmill tests allow an accurate assessment of the cardiorespiratory fitness of elderly males both before and after endurance training. The correlations among maximal test assessments of training response were high but the correlation with a submaximal test was weaker. Two explanations for this may be advanced. The submaximal and maximal tests may be measuring different aspects of the training response or the submaximal measure may be less reliable. A disadvantage of submaximal tests is that they may be less sensitive to training. Also selection of a fixed heart rate at which power output or $\dot{V}O_2$ is measured will impose varying degrees of stress due to variations in maximal heart rate among the elderly. The advantage of the submaximal test is that the result is not dependent on motivation. In young subjects attainment of a plateau in $\dot{V}O_2$ provides objective evidence that a true maximum was achieved. This objective marker is not available in many tests with elderly subjects. Further research concerning why elderly subjects fail to demonstrate a plateau is required.

4.2 Exercise Training and the Ventilation Threshold in the Elderly

Introduction.

The low correlation between maximal and submaximal measures of the training response observed in Chapter 4.1 suggests that perhaps $\dot{V}O_2max$ is not the sole determinant of aerobic performance. Indeed, in athletes the ability to perform maximal and submaximal exercise may be influenced differently by training (Costill, 1975). The association between $\dot{V}O_2max$ and distance running performance is lower than that observed between performance and the lactate threshold (Hagberg and Coyle, 1983). The lactate threshold refers to a point where, with increasing exercise intensity, there is a sharp rise in blood lactate which is usually accompanied by a disproportionate rise in ventilation relative to oxygen uptake. This inflection point has been termed the anaerobic threshold (Wasserman et al., 1973). However, to avoid implying knowledge of what the mechanism for the ventilatory rise is the term ventilation threshold will be used in this paper (Jones and Ehrsam, 1982).

Aging results in a decrease in both maximal oxygen uptake ($\dot{V}O_2max$) (Astrand et al., 1973) and the ventilation threshold (VeT). With exercise training $\dot{V}O_2max$ increases in all age groups including the elderly (Bassey, 1978; Grimby and Saltin, 1966; Smith and Serfass,

1981). VeT is increased with training in the young (Davis et al., 1979; Smith and Serfass, 1981), but the possibility of a change in VeT with training in men or women over 50 years of age has not been investigated.

In young subjects the VeT is typically in the range of 45 to 65 percent of $\dot{V}O_2max$ (Jones and Ehrsam, 1982). However, higher values have been reported for highly trained athletes (Costill, 1970) and for the elderly (Cunningham et al., 1984). The high values in the young endurance athletes are believed to result from genetic factors or long term, endurance training. It is unlikely that the same mechanism underlies the high relative threshold values reported for the elderly. A possible explanation lies in the suggestion by Wasserman and colleagues (1973) that the VeT will not fall below the $\dot{V}O_2$ required for daily activities such as walking ($\dot{V}O_2$ approximately 1 l/min) whereas, the $\dot{V}O_2max$ may continue to decrease with the lack of strenuous activity. As a result the ratio $VeT/\dot{V}O_2max$ will be increased in subjects with low fitness levels (low $\dot{V}O_2max$). Results from McLellan and Skinner (1981) support Wasserman's suggestion. They found a significant negative correlation ($r=-0.64$) between VeT and $\dot{V}O_2max$ in their study of sedentary young males.

Training studies in young subjects have demonstrated mixed results with $VeT/\dot{V}O_2max$ increasing or showing no significant change (Jones and Ehrsam, 1982). On the basis of their own findings and the results of previous studies (Costill, 1970), McLellan and Skinner suggest that a

plot of $VeT/\dot{V}O_2max$ relative to maximum oxygen uptake would be U-shaped. Training of individuals on the left arm of the U (low $\dot{V}O_2max$) would result in an increased $\dot{V}O_2max$ and lower relative threshold values. For subjects on the right arm of the U an increase in the relative ventilation threshold with little or no change in $\dot{V}O_2max$ would be postulated. The purposes of this study are: 1) to examine the effects of training on the ventilation threshold of the elderly; and 2) to examine the relationship between $VeT/\dot{V}O_2max$ and training in an elderly population.

Methods.

Testing Procedures.

Data were analysed for eighty-nine men who were randomly assigned to the control (n=44) or activity (n=45) groups. All data, including $\dot{V}O_2max$, maximum heart rate, and ventilation threshold were determined from the Stage I test. The ventilation threshold was identified as the final point before the ventilatory equivalent for oxygen began to increase without a corresponding increase in the ventilatory equivalent for carbon dioxide (Reinhard et al., 1979; Simon et al., 1983). Two observers independently checked the determination of the VeT on a sample of fifteen tests. VeT was similar with a small (<2%) and non-significant difference between the observers.

Statistical Analysis.

Student's t-tests were performed to determine if differences between baseline and at twelve month measurements within the control and activity groups were significant. SPSS multiple regression analysis (Nie et al., 1975) was used to determine the degree of association between VeT, VeT/$\dot{V}O_2$max, and $\dot{V}O_2$max at T2 as the dependent variables and the following independent (or explanatory) variables: baseline (T1) measures of VeT, VeT/$\dot{V}O_2$max and $\dot{V}O_2$max and control or activity group membership. A separate multiple regression was carried out using the training group to examine the association between change in VeT or VeT/$\dot{V}O_2$max and frequency of training plus the independent variables listed above.

Results.

The values of the physical and physiological measures made on control and activity groups subjects at baseline and 12 months are tabulated in Table 6. Mean baseline values were not significantly different between the two groups. Figure 1A illustrates the negative correlation ($r=-0.525$, $p<0.001$) between the baseline $\dot{V}O_2$max and the relative ventilation threshold. In addition, a U-shaped plot of the empirical relationship between VeT/$\dot{V}O_2$max and $\dot{V}O_2$max is superimposed on these data. Results from previous studies with young adult subjects (Davis et al., 1976; Davis et al., 1979; Farrel et al., 1979; Hughson

Table 6. Physical and physiological measures at baseline (T1) and twelve months (T2) for control and activity groups. Values are mean ± S.E.M.

Group		Age (yrs)	Height (cm)	Weight (kg)	$\dot{V}O_2$max (l/min)	V_ET (l/min)	$V_ET/\dot{V}O_2$max	Reserve Power (l/min)	HR at $\dot{V}O_2$max (beats/min)
Activity	T1	62.5 (0.5)	173.9 (1.2)	76.7 (1.4)	2.28 (0.07)	1.31 (0.03)	0.58 (0.02)	0.98 (0.06)	154 (3)
	T2	63.8 (0.5)	173.6 (1.2)	75.8 (1.40	2.70a,b (0.08)	1.39 (0.04)	0.52a,b (0.02)	1.31a,b (0.08)	155 (2)
Control	T1	61.8 (0.5)	173.4 (1.0)	82.3 (1.7)	2.34 (0.06)	1.39 (0.04)	0.60 (0.02)	0.94 (0.05)	155 (2)
	T2	63.0 (0.5)	173.6 (1.1)	82.7 (1.7)	2.45 (0.10)	1.38 (0.05)	0.58 (0.02)	1.07 (0.08)	153 (2)

a, difference between means at baseline and twelve months within a group is significant ($p<0.05$).
b, difference between groups at twelve months is significant after holding the baseline values constant ($p<0.05$).
Note: Reserve Power refers to the difference between $\dot{V}O_2$max and V_ET.

Figure 7A. Relative ventilation threshold ($\dot{V}eT/\dot{V}O_2max$) as a function of $\dot{V}O_2max$. Results from the current study (x) and earlier investigations are plotted with a hypothetical U-shaped curve which represents the expected relationship over the range of subjects with low to high cardiovascular fitness.

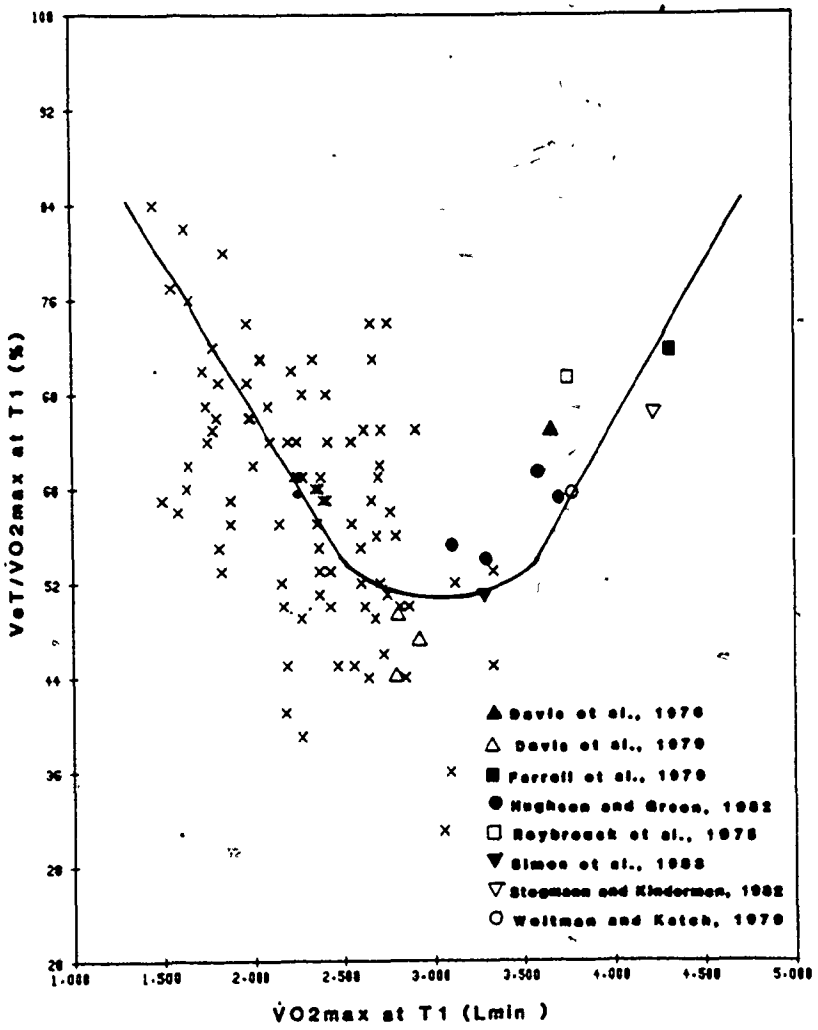
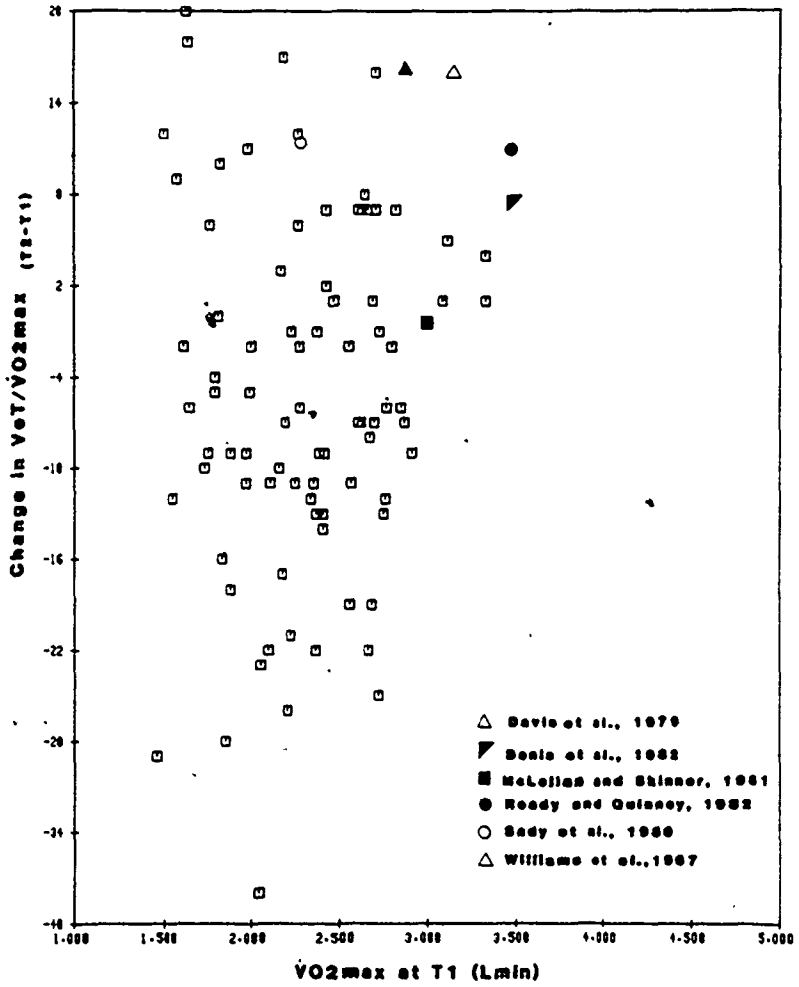


Figure 7B. The change in ventilation threshold with exercise training as a function of the initial $\dot{V}O_2$max. Results from the current study (▣) and earlier investigations are plotted.



and Green, 1982; Reybrouck et al., 1975; Simon et al., 1983; Stegmann and Kindermann, 1982; Weltman and Katch, 1979) have been included with those from the present investigation to define the U-shaped plot. If the relationship between $\dot{V}O_2max$ and $VeT/\dot{V}O_2max$ is U-shaped as suggested in Figure 7, our older subjects fall on the left arm of the U.

Adherence to the training program by the activity group was good with average attendance of 2.90 sessions per week over the year. The average training heart rate was 129.4 beats/min or 73 percent of heart rate reserve.

The changes observed from baseline to twelve months are summarized in Table 6. The training program was effective in increasing the $\dot{V}O_2max$ of the activity group with respect to the control group and with the initial value held constant. Maximum heart rate and body weight were not altered for either group. The change in VeT was not significant in either the control or experimental groups. When tested with the initial value of VeT at T1 held constant group membership, (independent variable) was not significantly related to VeT at T2 (dependent variable) (Table 6). When the $VeT/\dot{V}O_2max$ at T1 is held constant, the value at T2 is significantly lower in the activity group compared to the controls. The relationship between change in $VeT/\dot{V}O_2max$ and the initial value of maximal oxygen uptake (correlation not significant, $p>0.05$) is illustrated in Figure 7B. The correlation between the change in $\dot{V}O_2max$ and $VeT/\dot{V}O_2max$ was significant ($r=-0.43$). In addition,

results from previous training studies which examined the ventilatory or lactate threshold are plotted (Davis et al., 1979; Denis et al., 1982; McLellan and Skinner, 1981; Ready and Quinney, 1982; Sady et al., 1980; Williams et al., 1967). The correlation between $\dot{V}O_2$max and change in VeT/$\dot{V}O_2$max was not significantly different from zero. Finally, there was a significant increase in reserve ($\dot{V}O_2$max-VeT) at 12 months in the activity group only, and the change in the reserve value was significantly greater than that in the control group (the initial value was held constant). The association between training frequency and the change in VeT/$\dot{V}O_2$max was small (r=0.24, p>0.05).

Discussion.

The ventilation threshold was not significantly increased by exercise training in these elderly men despite a significant 18% increase in maximal oxygen consumption. The mean change in VeT with training was small (0.08 l/min). However, the range in response was very large (s.d.=0.30). This large variability in response to a training program appears to be a consistent problem in studying a diverse group like the elderly (Bafitis and Sargent, 1977). The lack of homogeneity for VeT/$\dot{V}O_2$max, in this age group, is reflected in the coefficient of variation of 10.6% for the young versus 17.2% for the elderly (Cunningham et al., 1984).

Two factors may have influenced the magnitude of the change in VeT observed. Other investigators have indicated that training intensity and frequency may affect the magnitude of the increase (Ready and Quinney, 1982; McLellan and Skinner, 1981)..The training intensity achieved by subjects in this subset of the study was variable. Heart rate was monitored during training sessions and averaged 73 percent of the difference between the maximum and resting heart rates. Training frequency was 2.9 sessions per week. Studies which have observed marked increases in VeT often employ a higher training frequency or training intensity. Ready and Quinney (1982) trained fit ($\dot{V}O_2max$=3.40 l.min-1) young (mean age 25 yrs) men four times a week for 9 weeks and observed a significant increase in VeT and in relative VeT (from 64.9% to 77.5% post training). Davis et al. (1979) vigorously trained (80 to 85% of $\dot{V}O_2max$, 4.1 session/week) a group of middle- aged (43+2.4 yrs) men for 9 weeks and observed a 7.6% increase in relative threshold. On the other hand, the extended period of training in the present study might have been expected to elicit changes in the VeT, particulary in light of the large change in $\dot{V}O_2max$.

The second factor in this study is age itself. Aging results in a multitude of changes, including an increased ratio of slow to fast twitch fibers (Larsson et al., 1978), a decreased lactate diffusion rate (Tzankoff and Norris, 1979), and a decreased respiratory sensitivity to CO_2 (Kronenberg and Drage, 1973). One suggestion is that the VeT threshold reflects a shift toward use of glycolytic muscle fibers. If

the proportion of these fibers in the muscle is decreased by aging the threshold may also be altered. Other mechanisms suggested to underlie the VeT include increased lactate or H+ ion concentrations leading to a rise in minute ventilation and $\dot{V}CO_2$. If aging does alter the time course of lactate or H+ ion diffusion or respiratory sensitivity, the VeT may be altered. Speculation about an interaction among aging, training, and VeT must await more information about the mechanism underlying the VeT and more data about the physiological alterations to the training process which result from aging.

Contrary to expectation, the change in relative threshold ($VeT/\dot{V}O_2max$) was not correlated with the subject's initial $\dot{V}O_2max$. The change in relative threshold however, was correlated to the change in maximal oxygen uptake ($r=0.43$, $p<0.05$). Our results therefore, support the hypothesis that changes in $VeT/\dot{V}O_2max$ for subjects with low initial fitness levels are due primarily to alterations in $\dot{V}O_2max$ with little or no change in VeT. This suggests that the physiological mechanisms which govern changes in $\dot{V}O_2max$ with training are not the same as those which determine the changes in VeT; or alternatively, a higher absolute training intensity must be achieved before VeT is increased.

4.3 Kinetics of the Cardiorespiratory Response to Exercise of the Elderly

Introduction.

Another factor which influences the ability to perform submaximal exercise is the rapidity with which the body responds to an increase in workload. If the supply of energy from aerobic metabolism lags the energy demanded by exercise the difference must be accounted for by anaerobiosis. This will lead to increased production of lactic acid and greater disturbance of homeostasis. Previous studies of the elderly have focused primarily on steady-state cardiorespiratory responses to dynamic exercise (Granath et. al., 1970; Niinimaa and Shephard, 1978; Robinson et al., 1975). Shock (1979) has hypothesized that the performance decrements observed with increased age are due to a decreased ability to co-ordinate and control the activity of interacting physiological systems. The age related decline in $\dot{V}O_2max$ is well documented (Skinner and Tipton, 1984) but few researchers have attempted to examine the ability of the elderly to increase oxygen uptake to meet the demands of an increase in exercise intensity. Early studies found heart rate, ventilation, blood pressure and gas exchange required more time to reach equilibrium in elderly subjects (Berg, 1947; Harris and Thomson, 1958; Robinson, 1938; Shock, 1961). In contrast, DeVries and colleagues (1982)

found no difference in the half time of response to work load change for $\dot{V}O_2$, $\dot{V}CO_2$ heart rate or ventilation between well trained young and old subjects.

A tight coupling between ventilation and $\dot{V}CO_2$ is observed in studies of young subjects (Diamond et al., 1980; Miyamoto et al., 1983; Whipp and Ward, 1980). Aging related changes which are expected to influence gas exchange and the cardiovascular response to exercise may uncouple this relationship. The objective of this study is to determine the effect of aging on the ability of the cardiorespiratory system to adapt to acute changes in work rate and on the relationship between $\dot{V}CO_2$ and ventilation.

Methods.

Subjects.

Six subjects volunteered and were fully informed of the risks and discomfort associated with all procedures before giving their written consent to participate in the study. Anthropometric measures including height, weight and the sum of skinfold thickness at 8 sites were made (see Chapter 3.0 for details). Pulmonary function including measures of vital capacity (VC), forced expiratory volume ($FEV_{1.0}$), and the maximum voluntary ventilation which could be maintained over 12 seconds at a self selected frequency were assessed.

Exercise Tests.

Testing included ramp function and step function tests on a Elema-Schonander cycle ergometer with workload controlled by a laboratory computer. Ramp function tests were preceeded by 5 to 7 minutes of no-load pedalling followed by a monotonic increase in work load (slope = 0.5 watts/sec) until a voluntary or symptom limited maximum was reached. Two maximal ramp tests were performed on separate days by each subject. In the step function tests a pattern of 4 minutes of no-load pedalling followed by an abrupt increase to the desired work level for 4 minutes was repeated for each work level. No-load pedalling corresponded to a work level of approximately 25 Watts. No-load pedalling was selected as the baseline condition to diminish the variability in the kinetic response (Maillard and Gautier, 1981). A total of 4 steps between no-load pedalling and 50 Watts were performed by each subject. Step function increases to 85, and 120% of the ventilation threshold were presented to the subject in randomized order over 2 laboratory sessions. A 10 to 15 minute rest period separated steps to different work levels. The variety of work load transitions were performed to allow comparison of responses at both relative and absolute exercise loads.

Data Collection.

Inspired and expired gas flows were measured with a turbine flowmeter (Alpha-tech) which was calibrated over the physiological range of flows with a 3 liter volumetric syringe. Volumes were computed by integration of the flow signal. The partial pressures of O_2 (fuel cell) and CO_2

infrared) were monitored continuously from ampling lines placed at the mouthpiece. Gas analyzers were calibrated before each test with samples of three mixtures of known composition (Scholander, 1947). The signals from the flow monitor and gas analyzers were sampled every 50 msec and the raw voltages stored for subsequent calculations. The delays between the flow and gas concentration signals were determined by measuring the time from onset of flow to attainment of 90% of the final gas concentration. Gas exchange was computed using the formulas published by Beaver and his colleagues for breath by breath gas exchange with inspired and expired flow measurements (1981) (See Appendix C). End-tidal gas fractions, peak inspiratory and expiratory flows, tidal and minute volume, and respiratory rate were determined for each breath. Heart rate was monitored from a modified CM5 lead and averaged over the duration of a breath.

Data Analysis.

The ventilation threshold (Jones and Ehrsam, 1982) was determined from the ramp test as the $\dot{V}O_2$ at which the ventilatory equivalent for oxygen ($\dot{V}E/\dot{V}O_2$) increased without an increase in the ventilatory equivalent for carbon dioxide ($\dot{V}E/\dot{V}CO_2$) (Wasserman and Whipp, 1975; Whipp et al., 1981).

The signal to noise ratio for the ventilation and gas exchange measurements was increased by averaging the responses over the 4 steps to 50 Watts and the two steps to each percent of ventilation threshold for each subject. Since the signal to noise ratio was too low to

describe the responses with an exponential equation, the time course at the onset of the step increase was characterized by the time to reach 50% of full response (t1/2). The t1/2 was graphically determined for $\dot{V}O_2$, $\dot{V}CO_2$, and ventilation (Figure 8). The fall in resolution due to averaging over the duration of a breath made determination of the very rapid kinetics of the heart rate response impossible. In addition unreliable triggering of a heart rate monitor in some initial tests resulted in loss of data. The rate of response to the ramp function increase was assessed as described by Whipp et al. (1981). Briefly, the increase in oxygen consumption lags the rise in work load by a constant value. This lag time is equal to the time constant of the response plus any delay time and is termed mean response time (MRT) by Linarsson (1974).

The correlation coefficients among time constants for the gas exchange variables were computed to test the hypothesis that aging uncouples the association between ventilation and $\dot{V}CO_2$ observed in young subjects (Whipp and Ward, 1980)

Results.

The physiological characteristics and responses to maximal exercise of these subjects (Table 7) are comparable to average values for this age group (Shephard, 1978). Fifty percent of the subjects demonstrated a plateau in oxygen consumption (<2ml/kg/min change) over the final 30

seconds of the test. The test was halted due to fatigue in all cases. The mean maximum heart rate (165 b/min) was well above the rate predicted by the "rule of thumb" equation (220-age in years). The average ventilation threshold relative to maximal oxygen uptake is higher (64%) than that reported for young subjects (Jones and Ehrsam, 1982), but is comparable to that observed for another sample of elderly men (see Chapter 4.2). The mean values (averaged over the final 30 seconds at the specific power output) for gas exchange and heart rate variables are displayed in Table 8. The maximum ventilation attained during exercise was 98% of the maximum measured at rest. The correlation between the resting and exercise maximum ventilation measures was 0.70 ($p < 0.05$).

The mean rates of response for all subjects to step increases in exercise of varying intensities are illustrated in Table 8. A representative tracing obtained from a step work transition for one subject is illustrated in Figure 8. The half time response was not significantly different ($p < 0.05$) among varying exercise intensities. However, the response to a ramp function appears to be faster than that observed with a step function. The values for the step increases are half times, which if the function is a simple exponential, would be approximately 70% of the mean response time observed with the ramp function increase. The half time values which we observe are approximately 90% of the mean response time.

TABLE 7. Physical characteristics of subjects and responses to maximal cycle ergometer exercise. Values are means (standard deviation).

	Age (yrs)	Weight (kg)	Height (cm)	*Skinfolds (mm)	FVC (L)	$FEV_{1.0}$ (L)
Mean	65.2	83.3	173.2	117.7	3.71	2.92
(sd)	(1.9)	(5.4)	(4.7)	(20.2)	(0.71)	(0.45)

	$\dot{V}O_2max$	VeT.	HRmax	$\dot{V}E$max	MVV
Mean	2.93	1.87	165	80.7	82.1
(sd)	(0.38)	(0.18)	(8)	(20.4)	(28.3)

* Sum of skinfold measurements at 8 sites.

TABLE 8. Gas exchange and heart rate during step function increases in power output. VeT, ventilation threshold.

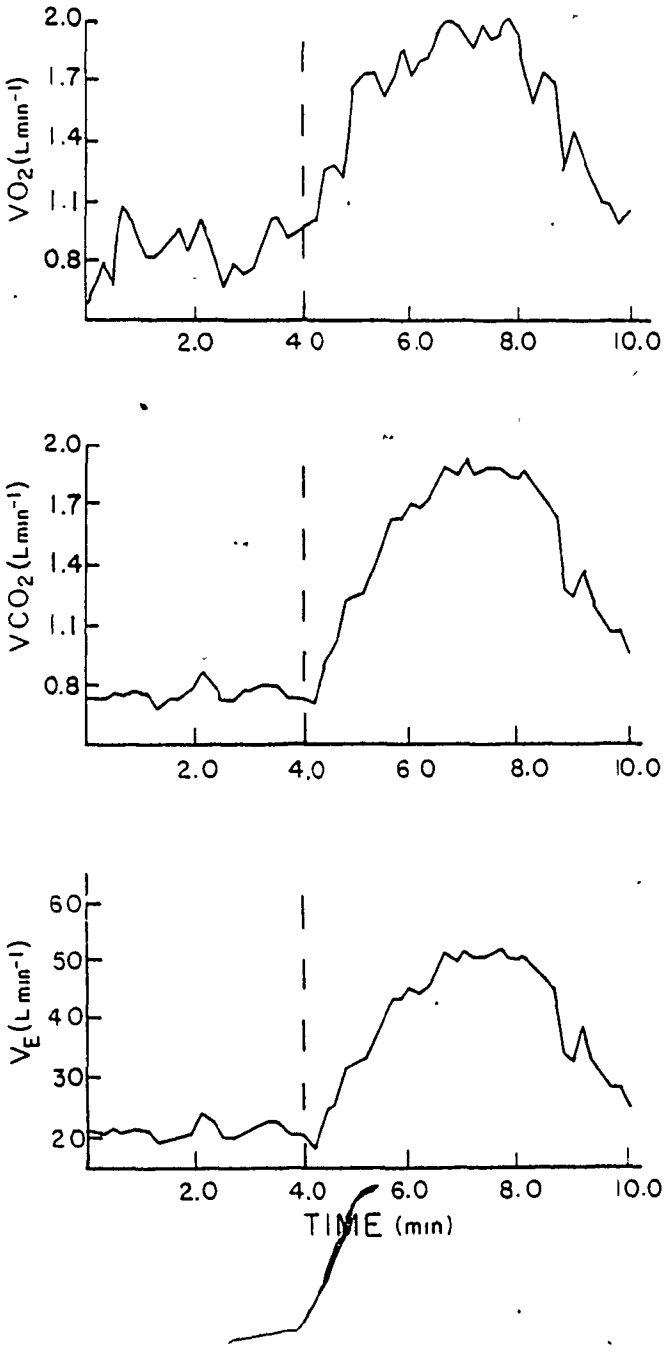
Variable	50 Watts	85% VeT	120% VeT
$\dot{V}O_2$ (l/min)	1.16 (0.16)	1.72 (0.19)	2.25 (0.23)
$\dot{V}CO_2$ (l/min)	1.04 (0.08)	1.37 (0.17)	2.14 (0.18)
$\dot{V}E$ (l/min)	28.0 (4.5)	36.7 (4.0)	50.2 (12.8)
*RER	0.89 (0.09)	0.80 (0.05)	0.94 (0.08)
HR (bpm)	110 (6)	119 (7)	128 (11)

*RER, respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$)

TABLE 9. One half response times (t1/2, sec) for step function increases to 50 Watts, 85 and 120% of the ventilation threshold. Mean response time (MRT) obtained from a ramp function test to maximum. Values are means (n=6) ± standard deviation.

Variable	Ramp	Step		
	(MRT)	50W	85%	120%
$\dot{V}O_2$	50.8 (11.0)	55.4 (5.4)	56.7 (3.0)	51.7 (5.9)
$\dot{V}CO_2$	60.3 (13.9)	61.9 (6.9)	63.1 (5.5)	62.2 (7.6)
$\dot{V}E$ (l.min-1)	66.7 (16.5)	71.3 (6.3)	70.6 (4.2)	62.5 (12.0)
r, $\dot{V}O_2$-$\dot{V}E$	0.80	0.65	0.60	0.43
r, $\dot{V}CO_2$-$\dot{V}E$	0.90	0.98	0.64	0.61

Figure 8. Representative tracing (single subject) of the time course of gas exchange and ventilation in response to a step increase from no load pedalling to 120 Watt power output.



Discussion.

The major finding of this paper is that the rate at which an elderly subject responds to an increase in exercise intensity is slower than the values reported for young adults. The mean values for t1/2 from studies of young subjects (20-35) are displayed in Table 10. The values were converted where necessary from time constants (τ) by multiplying by 0.693 and adding the reported time delay.

We were unable to fit an exponential equation to our data. This problem may stem from three sources: 1) The magnitude of step increases possible with the elderly is small because of their decreased $\dot{V}O_2max$ and low ventilation threshold. Increases to power outputs above the threshold produce a continual rise in gas exchange which makes fitting a simple exponential curve impossible. As a result of the limit imposed by the low VeT in elderly subjects the signal size must be small; and 2) the amount of noise was large due to wider variations in breathing pattern and because the gas exchange algorithm which we employed did not compensate for changes in lung gas stores. This source of error may be greater in the elderly relative to the young because of increases in residual lung volume; and finally, 3) the pattern of increase may not be exponential in the elderly. This does not appear to be true from inspection of individual data records of our subjects. However, there is considerable variation in the shape of each subject's curve between

TABLE 10. One half response times (sec) calculated from values reported in the literature for young adult subjects.

Reference	Mean Age	Transition	$\dot{V}O_2$	$\dot{V}CO_2$	$\dot{V}E$
Diamond et al., 1977.	26.3	R-W	32	41	47
		W-W	35	47	52
Hagberg et al., 1980.	30.0	R-50% $\dot{V}O_2$max	32.2	44.0	44.5
Hughson and Morrissey, 1982.	19.3	R-80% AT	26.8	37.4	39.0
		40-80% AT	40.2	43.7	59.4
		40-120% AT	44.0	48.8	69.5
Linnarsson, 1974.	24.6	0-65% $\dot{V}O_2$max	30.1	44.4	46.5

repeated tests. The one half response time for $\dot{V}O_2$ reported by DeVries and colleagues (1982) for their elderly subjects (30.0 secs) is substantially less than that observed in the present study (mean t1/2 $\dot{V}O_2$=54.6 secs). Response times are decreased by improvements in physical condition. Hagberg and his colleagues (1980) found that a 24% increase in $\dot{V}O_2$max was accompanied by an decrease in half time response for $\dot{V}O_2$ of 25% during transitions to the same absolute workload. The five elderly subjects in DeVries' study were competitors in Senior Olympic distance running while our subjects were sedentary. This difference is reflected in the mean maximal $\dot{V}O_2$ which was 43.8 for DeVries subjects versus the 35.2 ml/kg/min average for our subjects.

There is disagreement about the effect of prior exercise on the response time. Davies et al. (1972) and DiPrampero et al. (1970) reported faster responses to work load changes if the transition was made from prior exercise rather than from rest. Others (Diamond et al., 1977; Casaburi et al., 1977) have reported no difference in response time. Hughson and Morrissey (1982) found that transition time was increased when step increases originated from 40% of the anaerobic threshold compared to steps starting from rest. Some authors (Hughson et al., 1982) report that response times are slower during transitions to high workloads versus lower exercise intensities while others (Diamond et al., 1977) report that response times are stable across step increases of varying intensity. We observed a tendency for response times to increase but this did not achieve statistical significance.

Preliminary studies confirmed the findings of Swanson et al. (1981) that without a correction for nitrogen flow the calculation of change in lung stores from difference in measured inspired and expired volumes is very sensitive to errors. Since accurate measurement of nitrogen was not available we did not correct our gas exchange values for changes in lung stores.

The correlation between $\dot{V}E$ and $\dot{V}CO_2$ at low power output is comparable to values reported for young subjects but decreased with exercise intensity. This suggests that other inputs may influence ventilatory control in the elderly as power ouput increases. Possible inputs include information from receptors in the muscles or increased central drive.

The elderly subjects in this study used a large proportion of their maximum voluntary ventilation during exercise. Three explanations for this finding may be advanced. First, the maximum exercise ventilation was measured as an average of the last 12 breaths. This represents only approximately 20 seconds which may be a brief enough time span to attain a large fraction of the 12 second MVV. Second, the expiratory resistance of the exercise ventilation system is very low, which permits a higher ventilation for a given effort than systems which incorporate a breathing valve. Finally, age related decrements in pulmonary function may decrease the ventilatory reserve.

4.4 Determinants of The Training Response.

Introduction.

The decreased ability of the elderly to perform aerobic exercise is attributed to decreased habitual physical activity and increased age. Declines due to decreased activity should be reversible with physical training. However, there is uncertainty about the ability of the elderly to adapt to a training stimulus (Raven and Mitchell, 1980). A general decrease in adaptability to stimuli with increased age has been hypothesized (Bafitis et al., 1977) and increases in $\dot{V}O_2max$ of 0.0 to 38.0% as a result of training have been reported (Benestad, 1965; Barry et al., 1966). The magnitude of the training response in young adults is related to their initial physiological condition, their level of physical activity before entering the study, the training stimulus applied (intensity, frequency, and duration of training sessions), and the duration of the training program (Pollock, 1973). The role of these factors in determining the training response of elderly men has received little study (Badenhop et al., 1983; Devries, 1971; Sidney and Shephard, 1978) and the interaction between these variables has not been explored. Conflicting conclusions about the effect of training intensity in the elderly have been reported. Badenhop et al. (1983) reported that high or low intensity training produced the same gain in $\dot{V}O_2max$ while Sidney

and Shephard (1978) found that high intensity training resulted in much larger gains than were evident with a low intensity program.

At present little is understood of the factors which will predispose an elderly person to significant changes in cardiovascular fitness following a program of exercise training. The ability to respond to training may be an important determinant of aerobic capacity in this segment of the population. The purpose therefore, of this section of the thesis is to describe the determinants of the response to exercise training in the elderly.

Methods.

Subjects. Two hundred and twenty four men were recruited as outlined in the general method section (Chapter 3.1). The men were randomly allocated to a control (n=111) or activity (n=113) group. Twenty four men refused final maximal testing and of those who completed the final maximum test an additional 12 men dropped out of the training program and therefore were not included in this analysis. This resulted in a decrease in sample size to 100 control subjects and 88 in the activity group.

All subjects (mean age 62.3 yrs.) underwent a battery of physiological tests at entry to the study (T1), and twelve months after entering the study (T3). The test battery included a medical history,

anthropometric measurements, a 12 lead electrocardiogram, spirometry measures, a Stage I treadmill test, and one of the following three alternative second tests done up to 1 week later, a repeat of the Stage I test, a modified version of the Stage I, or a Stage II test. The reason for halting the stress test (RST) was recorded (Cunningham and Rechnitzer, 1974). For purposes of this analysis, the reasons were grouped into two classes 1) fatigue 2) all other reasons which included ECG abnormalities, angina, syncope, a fall in systolic blood pressure, and claudication. The data for the baseline test session were gathered over 3 visits to the laboratory. Subjects were habituated to treadmill walking on their first exposure to the laboratory and underwent maximal tests on their second and third visits. The reliability of the $\dot{V}O_2max$ measures on elderly subjects is considered elsewhere (Chapter 4.1). Training induced changes in physiological function were assessed using values from the treadmill test where $\dot{V}O_2max$ was highest regardless of which test protocol was employed. This approach minimizes the possibility of inflating the difference between pre and post training measures by underestimating the baseline values. Gas exchange was calculated using the open circuit method as outlined in Chapter 3.3.

Initial $\dot{V}O_2max$, $FEV_{1.0}$, and the sum of skinfold thicknesses (Σ skinfolds), and the reason for halting the stress test (RST) were employed as descriptors of a subject's initial physiological state. Activity over the year previous to entering the study was assessed using the Minnesota Leisure Time Activity questionnare (Taylor et al., 1978).

Activities requiring high energy expenditures (greater than 5.0 times the resting metabolic rate) may produce a training effect and therefore reduce the trainability of our subjects.

Training Program.

Thirty minute long walk/jog training sessions were offered three mornings a week. Training intensity was based on the results of the initial Stage I test using the formula of Cunningham et al. (1974) (See Appendix C).

This exercise prescription was revised for all subjects on the basis of another Stage I test carried out 6 months following the initial test. If rapid progress was evident after 3 or 9 months an additional test was performed to allow updating of the exercise prescription. Subjects were assigned to exercise leaders in groups of 10 to 15. Exercise leaders taught the men to palpate their heart rate (Pollock et al., 1972). Subjects were encouraged to start slowly and work toward matching their target heart rate over the first 3 to 4 weeks of training. Each training session consisted of a 10 to 15 minute warm-up, approximately 30 minutes of walking or jogging at a pace set to elicit the prescribed heart rate, and a 10 minute warm-down. The subjects recorded distance travelled, time spent walking or jogging and the pre-, mid- and immediately post-exercise heart rates for both supervised sessions and any additional training which they undertook. During the supervised sessions exercise leaders frequently checked pulse rates to ensure accuracy in recording the heart rate values.

Data Analysis.

Differences between control and activity groups on descriptive baseline measurements, including $\dot{V}O_2max$, height, weight, age, and the sum of skinfold thickness measures were statistically evaluated using Student's t-tests. To establish that a training response did occur as a result of this training program multiple regression was used to test the hypothesis that the difference between the control and activity groups at the final (T3) testing was significant after controlling for differences on the initial (T1) test (Donner and Cunningham, 1983).

The subsequent analyses, which address the question of what factors determine the response to training will be restricted to members of the training group. The relationships between measures of interest were illustrated by computing Pearson product-moment correlation coefficients. The simplest presentation of the response to training is to calculate the difference between pre and post training measures of $\dot{V}O_2max$, however, the use of change scores has been criticized because of their poor reliability (low correlation coefficient for repeated measures) and potentially low power (Dotson, 1973; Linn and Slinde, 1977). An alternative method of identifying the factors related most strongly to the training response is to examine the association between the explanatory variables of interest and the final $\dot{V}O_2max$, after the influence of initial $\dot{V}O_2max$ is held constant. Results will be presented using the multiple regression method of examining the effect of various factors on the training response.

Results.

One year of endurance training resulted in a 13.2% increase in maximum oxygen consumption (Table 11). This improvement in cardiorespiratory function was accompanied by an increase in maximum minute ventilation (15.0%) and no change in maximum heart rate, respiratory exchange ratio, or weight. The increases in $\dot{V}O_2$max and maximum $\dot{V}_E$ are significant with respect to the baseline values and compared with the change observed in the control group. When those subjects whose baseline test was halted for reasons other than fatigue (n=10)(eg. angina, ST segment depression) are eliminated from the analysis the increase in $\dot{V}O_2$max with training is 13.6%. However, the average increase in $\dot{V}O_2$max of subjects with a symptom limited test was 2.0 versus the 3.9 ml/kg/min for subjects whose test was halted by fatigue. The initial maximal heart rate for the combined control and activity groups increases from 156 to 158 with removal of data from subjects with a symptom limited maximum. The scattergram in Figure 9 illustrates the relation between $\dot{V}O_2$max values after training versus before training for all subjects in the activity group. The majority (58%) of subjects who demonstrated a decrease in $\dot{V}O_2$max over the year experienced a symptom limited rather than fatigue limited maximal test at entry and/or completion of the study.

Table 11. Comparison between control and activity groups at baseline (T1) and twelve months later (T2). Maximal values for $\dot{V}O_2$, $\dot{V}E$, HR, and respiratory exchange ratio (RER) were obtained from the treadmill test which produced the highest $\dot{V}O_2$max at each time point. Data from subjects who did not complete testing at both time points and from activity group members who dropped out of training is excluded. Heavy AMI score indicates amount and intensity of activity requiring more than 5 times the resting metabolic rate. Means ± SE.

Variable	T1		T2	
	Activity (n=88)	Control (n=100)	Activity (n=88)	Control (n=100)
$\dot{V}O_2$max (ml/kg/min)	30.8 ±0.6	29.6 ±0.6	34.5[a] ±0.8	30.4 ±0.7
$\dot{V}E$max (l/min)	82.1 ±2.2	83.4 ±2.2	94.4[a] ±2.6	87.6 ±2.5
RERmax	1.08 ±0.01	1.10 ±0.01	1.10 ±0.01	1.10 ±0.01
HRmax (bpm)	158 ±2	155 ±2	158 ±2	157 ±2
Weight (kg)	78.1 ±1.1	79.8 ±1.1	77.6 ±1.1	80.0 ±1.1
Heavy AMI	100.3 ±13.0	79.0 ±10.4	233.5 ±17.6	144.9 ±20.3
$FEV_{1.0}$ (l/sec)	2.83 ±0.05	2.86 ±0.05	2.90 ±0.09	2.82 ±0.05
Σ skinfolds (mm)	112.6 ±8.5	111.8 ±7.4	105.0 ±3.4	117.3 ±7.5

[a] Values at T2 are significantly different with respect to the initial value and between groups, $p<0.05$.

TABLE 12. Description of training program. Mean values, standard deviation, range (low, high) for each quarter year of training.

Variable	Time Period			
	0-3 months	3-6 months	6-9 months	9-12 months
Workout Frequency (Sessions/wk)	2.6 ± 0.9 (0.4, 7.0)	2.4 ± 0.9 (0.2, 6.8)	2.3 ± 0.9 (0.8, 6.8)	2.4 ± 0.9 (0.2, 6.9)
Post-exercise Heart Rate (bpm)	126 ± 16 (84, 160)	130 ± 18 (80, 165)	132 ± 18 (80, 165)	131 ± 18 (80, 167)
% Heart Rate Reserve	66 ± 14 (14, 103)	71 ± 17 (26, 117)	71 ± 17 (30, 111)	71 ± 17 (24, 117)
% Prescribed Heart Rate	98 ± 9 (72, 125)	101 ± 10 (69, 131)	101 ± 11 (69, 129)	101 ± 12 (65, 126)
Speed (km/hr)	6.3 ± 1.2 (3.2, 10.3)	6.6 ± 1.5 (3.2, 10.7)	6.8 ± 1.5 (3.2, 11.2)	7.0 ± 1.6 (3.1, 11.3)

Good adherence to the training program is reflected in the high percent of prescribed heart rate achieved and mean frequency of attendance (Table 12). The mean duration of the walk/jog portion of the training sessions remained constant at 30.0 + 0.2 minutes over the year. An increased ability to perform aerobic activity is indicated by the progressive increase in average speed of walking or jogging. A slight decrease in the frequency of attendance after the first quarter year is evident but this change is not statistically significant. The correlations between the measures of training intensity (percent of prescribed heart rate and percent of heart rate reserve) ranged from 0.91 to 0.96 over the four quarters of training. Percent of heart rate reserve was employed to describe training intensity since this allows comparision of results between this and previous studies of the effect of training intensity.

The simple correlation coefficients among the independent and dependent measures are presented in matrix form (Table 13). The negative relation between the initial $\dot{V}O_2max$ and change in $\dot{V}O_2max$ is expected, as is the correlation between initial and final VO_2max values. Three baseline measures ($FEV_{1.0}$, heavy AMI, and the sum of skinfold thicknesses) are correlated to the initial $\dot{V}O_2max$ value. The association between lung function and $\dot{V}O_2max$ suggests that pulmonary function may influence aerobic function in the elderly, this is supported by the significant correlation between $FEV_{1.0}$ and participation in high intensity leisure time activities. The negative

Figure 9. Scatterplot of $\dot{V}O_2max$ values, for subjects who were members of the training group, obtained from the best test performed at entry (T1) and at completion of one year of training (T2). Line of identity is drawn to clarify the relation between pre and post training values (n = 88).

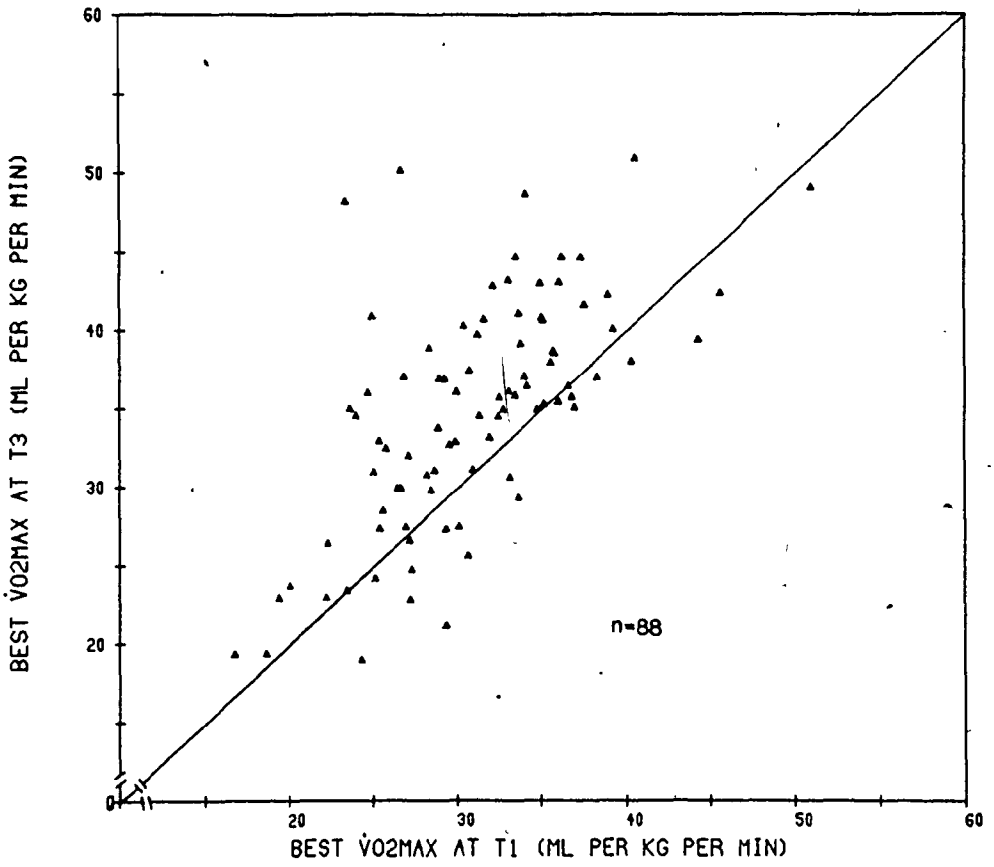


Table 13. Correlation matrix for indices of initial condition ($\dot{V}O_2max$, FEV1.0, Σskinfolds, RST), past activity (Heavy AMI), and training stimulus (% HR reserve, frequency of training) with training induced change in $\dot{V}O_2max$ (Delta $\dot{V}O_2max$) and post training $\dot{V}O_2max$ ($\dot{V}O_2max$, T2). Measures made at entry to the study are indicated by T1.

	$\dot{V}O_2max$, T1	$\dot{V}O_2max$, T2	Delta $\dot{V}O_2max$	Frequency	%HR Reserve	HAMI, T1	FEV1.0, T1	Σskinfold, T1
$\dot{V}O_2max$, T2 (ml/kg/min)	0.65 (0.001)*							
Delta $\dot{V}O_2max$ (T2-T1)	-0.21 (0.023)	0.60 (0.001)						
Frequency (sessions/wk)	-0.06 (0.0272)	-0.08 (0.221)	-0.04 (0.362)					
% HR Reserve (%)	-0.001 (0.496)	0.13 (0.118)	0.16 (0.062)	-0.35 (0.001)				
HAMI, T1	0.23 (0.017)	0.02 (0.409)	-0.20 (0.028)	-0.01 (0.466)	-0.14 (0.095)			
FEV1.0, T1 (L)	0.33 (0.001)	0.24 (0.014)	-0.04 (0.346)	0.005 (0.481)	-0.08 (0.220)	0.39 (0.001)		
Σskinfold, T1 (mm)	-0.26 (0.008)	-0.11 (0.153)	0.12 (0.122)	0.03 (0.402)	0.01 (0.463)	-0.11 (0.152)	-0.05 (0.326)	
RST, T1	-0.43 (0.001)	-0.43 (0.001)	-0.10 (0.165)	0.24 (0.011)	-0.01 (0.467)	-0.14 (0.097)	-0.06 (0.275)	0.30 (0.002)

* values in parenthesis are p values for significance of the correlation coefficient.

Table 14. Multiple regression of final (T2) maximum oxygen uptake on several independent variables. RST, T1 is the reason for stopping the maximal treadmill test at baseline, Heavy AMI, T1 is the score for physical activity above the 5 Met level in the year preceeding the study. Frequency is the average number of exercise sessions attended per week. %HR reserve measures the intensity at which the subject trained. Var., variance.

Depen. Variable.	Indepen. Variable	p value*	Delta % Var.	Total Var. Explained
$\dot{V}O_2max$, T2	$\dot{V}O_2max$,T1	0.001	42.1	
	RST, T1	0.012	2.8	
	HAMI, T1	0.092	1.8	
	%HR Res.	0.133	1.2	
	$FEV_{1.0}$, T1	0.277	0.9	
	Σskin., T1	0.264	0.8	
	Frequency	0.538	0.2	
				49.8

*p-value is the probability of that explanatory variable being associated with the dependent variable (after the effect of the other dependent variables is held constant) by chance.

association between frequency of attendance at exercise sessions and training intensity was unexpected.

A stepwise multiple regression analysis of potential correlates of the training response in experimental group subjects (Table 14) reveals that the $\dot{V}O_2max$ at the final test is significantly associated with the reason for stopping the initial test. The subjects who stopped for reasons of fatigue had a higher $\dot{V}O_2max$ at the final test and a larger change in $\dot{V}O_2max$ with training than men with symptom limited stress tests. The effect of high intensity activity over the year previous to entering the study just failed to reach statistical significance. Although the F statistic for reason for stopping the test was significant once the initial $\dot{V}O_2max$ was held constant it accounted for a very small amount of the variation explained (2.8%). When $\dot{V}O_2max$ at entry is dropped from the analysis $FEV_{1.0}$ is a significantly associated with the final $\dot{V}O_2max$.

Discussion.

An average increase of 13% in $\dot{V}O_2max$ as a result of training indicates that the elderly are quite responsive to an exercise stimulus. The best predictor of what an elderly subject's $\dot{V}O_2max$ will be after one year of training is his initial $\dot{V}O_2max$. Once this source of variation is controlled for the variables which are traditionally used

to describe the training stimulus explain little of the remaining variance. However, subjects whose test was symptom limited will not gain as much from a training program as will subjects whose test was halted by fatigue. It might be expected that subjects with symptom limited tests would demonstrate smaller improvements in $\dot{V}O_2$max because of a lower training intensity. However, these subjects demonstrate a smaller response to training even if the effect of differences in training intensity, frequency and initial $\dot{V}O_2$max are held constant through use of the multiple regression technique.

DeVries (1971) examined the relation of change in $\dot{V}O_2$max estimated from a submaximal exercise test with training intensity and initial fitness. A multiple regression analysis indicated that 41% of the variance in the change score could be explained by the initial predicted $\dot{V}O_2$max and the percent of heart rate range at which the subject trained. The results of this study are subject to two criticisms ; 1) the reliability of change scores is low (Dotson, 1973) and; 2) because use of a predicted $\dot{V}O_2$max score, which has low reliability and a systematic error (Sidney and Shephard, 1977), further reduces the accuracy of the results.

On the basis of previous research with young subjects we expected that training intensity would have a positive effect on the change in $\dot{V}O_2$max with training. Although the simple correlation coefficient was in the expected direction the effect observed with multiple regression

analysis was quite small and not statistically significant. Previous studies using subjects in the same age range as our subjects have produced conflicting results. DeVries found a weak correlation (r=0.383) between percent of heart rate range during training and change in $\dot{V}O_2$max estimated from the Astrand cycle ergometer test. Sidney and Shephard (1978) reported that walking or jogging at a high intensity (training heart rates from 140 to 150 bpm) produced larger gains than low intensity (heart rates from 120 to 130 bpm) training. Unfortunately their results are based on prediction of $\dot{V}O_2$max from a submaximal cycle ergometer test and the division of subjects into high and low intensity training groups was carried out on a post hoc basis. The large coefficient of variation (14.5%) of cycle ergometer prediction of $\dot{V}O_2$max makes evaluation of change in $\dot{V}O_2$max less accurate. In agreement with our findings Badenhop et al. (1983) found that elderly subjects who were randomly assigned to a high (60% of heart rate reserve) or low (38% of heart rate reserve) intensity cycle ergometer training program demonstrated the same percent increase in directly measured $\dot{V}O_2$max.

Frequency of training did not affect the magnitude of the training response. All subjects were encouraged to attend 3 supervised exercise sessions per week and the small standard deviation (0.71) around the mean value (2.45) suggests that perhaps the range of values is not large enough to perform a meaningful correlation analysis.

A high activity level before entering a training program should reduce the increment in $\dot{V}O_2max$ which is observed. This hypothesis is confirmed by the negative correlation between change in $\dot{V}O_2max$ and heavy AMI score. However, once the initial $\dot{V}O_2max$ value is accounted for the level of previous activity is not a significant determinant of the final $\dot{V}O_2max$. Past activity is important in the trainability of elderly men only through its effect in determining the initial $\dot{V}O_2max$.

Caution in interpreting the relative importance of past activity levels (heavy AMI) and other measures such as $\dot{V}O_2max$ as determinants of the training response is advised. The correlation between an independent and dependent variable is attenuated by errors in measuring the independent variable (Pedhazur, 1982, p 230). The measurement error for $\dot{V}O_2max$ is probably smaller than that of a recall questionnare measure of activity. As a result the observed correlation between training change, or $\dot{V}O_2max$ at T3 after controlling for initial $\dot{V}O_2max$, and past activity is probably attenuated more than the correlation between $\dot{V}O_2max$ at T3 and initial $\dot{V}O_2max$.

Why do the traditional factors (training intensity, and initial fitness) account for so little of the variation in training response? There may be wide variations in the adaptability of each individual that are not captured by our measures. The negative effect that a symptom limited test has on the training response suggests cardiac or peripheral vascular disease reduces the ability to benefit from exercise training.

Another possibility is that we have not measured the true training stimulus. Alternate methods (% of prescribed heart rate or post exercise heart rate) of quantifying the exercise stimulus intensity did not increase the amount of variance in response which was explained. Retirement allows much more leisure time for activities such as golfing, gardening, skating or skiing which may act as training stimuli. However, the leisure time activity questionaire measures this increase and we found that the change in activity level over the year of training (High activity score at T1 - high activity score at T2) accounted for only 1.3 % of the variation in $\dot{V}O_2max$ at final testing after the effect of the initial $\dot{V}O_2max$ value is held constant.

In summary one year of training does effect a significant increase in the aerobic fitness of elderly men. The traditional determinants of the training response explain little of the variation in the magnitude of the response. The weak, non-significant effects observed are in the direction predicted from previous studies which employed young subjects. Subjects with symptom limited maximal stress tests demonstrate smaller gains with training than do men who stop exercise because of fatigue. The majority of the variation in training response remains unexplained.

4.5 Cardiovascular effects of endurance training in the elderly

Introduction.

A decrease in maximal cardiac output due both a lower maximum heart rate and a smaller maximal stroke volume is reported to be a major factor in the decreased $\dot{V}O_2max$ of the elderly (Gerstenblith et al., 1976). However, while the ability of elderly subjects to respond to an endurance training stimulus by increasing $\dot{V}O_2max$ has been established (Badenhop et al., 1983; Shephard, 1978) the role of cardiovascular adaptations in this process is unknown. Studies with young adult subjects indicate that an increased oxygen uptake may be associated with increased $CaO_2-C\bar{v}O_2$ or with increased cardiac output (Cunningham et al., 1975; Thomas et al., 1981). The ability to effect changes in either of these variables in elderly subjects has been questioned (Gerstenblith et al., 1976; Shephard, 1980). Previous studies of the effect of exercise training on the cardiovascular system in elderly subjects suffer from inadequate description of the training stimulus and small sample sizes. Cardiac output at a given $\dot{V}O_2$ is variously reported to remain unaltered (Hartley et al., 1969), to decrease (Niinimaa and Shephard (1978), or increase (Schocken et al., 1983). The purpose of this study is to document the effects of endurance training on the function of the cardiovascular system in elderly male subjects.

Methods.

All subjects were volunteers from the community who were retiring from their full time occupations. Cardiac output was determined in one hundred and forty five men who responded to contact through their company personnel offices, newspaper advertisements and by word of mouth. All subjects were fully informed of the possible risks and discomfort associated with each procedure before consenting to participate.

Study Design.

Subjects were randomly assigned to a control or exercise training group. All subjects were evaluated at entry and 12 months later with the battery of tests outlined in Chapter 3.0. A stage II (Jones and Campbell, 1982) treadmill test was used to determine the cardiorespiratory, including cardiac output, response to three submaximal exercise levels. Loads were selected to elicit heart rates corresponding to 50 (low), 65 (medium), and 80 (high) percent of the difference between resting and maximum heart rates. The maximum heart rate and the relationship between heart rate and treadmill grade were determined from a previous incremental exercise test that was sustained to an effort or symptom limited maximum (Jones and Campbell, 1982). A progressive test to maximum was performed following completion of the third submaximal exercise level of the Stage II test. The reason for halting the test was recorded (Cunningham et al., 1974). Each submaximal

exercise level was sustained for 5 to 6 minutes with 5 minutes of rest between work levels. Gas exchange ($\dot{V}O_2$, $\dot{V}CO_2$) was calculated from inspired minute ventilation (Parkinson-Cowan dry gas meter), and measures of the mixed expired fractions of O_2 (fuel cell analyzer) and CO_2 (infrared analyzer) which were made after a cardiovascular steady-state (<5 beats.min-1 change from minute 2.75 to 3.75 or 3.75 to 4.75) was achieved.

Cardiac output was measured with the indirect CO_2 Fick method at each of the submaximal exercise intensities. The reliability and reproducibility of this technique have been tested and confirmed in this laboratory using young to middle aged subjects (Wolfe et al., 1978). The mixed venous concentration of CO_2 was determined by the rebreathing method (Jones and Campbell, 1982). The Bohr equation was used to estimate arterial PCO_2 from the dead space (V_D) prediction equation of Bradley and her associates (V_D=0.8698 age(yrs) - 1.29 height(cm) - 0.4509 $\dot{V}CO_2$(ml.min-1) + 20.02$\dot{V}E$(l.min-1) + 1291/(breathing frequency) + 270.4, r=0.83, Syx(ml)=69.9) (Bradley et. al., 1976). Gas contents were calculated from gas tensions using the CO_2 dissociation curve of McHardy as modified by Jones et al. (1979). Data were corrected to the individual's hemoglobin concentration using values measured from venous blood sampled at rest. An arterial O_2 saturation of 95% was assumed (Altman and Dittmer, 1974).

Training.

Subjects in the training program were offered 3 medically supervised exercise sessions per week as outlined in Chapter 3.3. Training heart rate was calculated as a fraction of the range between resting and maximum rates. $\dot{V}O_2max$ and maximum heart rate were determined on the initial Stage I test.

Data Analysis.

The multiple regression technique was employed to evaluate the effect of training on $\dot{Q}$, SV, $CaO_2-C\bar{v}O_2$ and heart rate while controlling for the initial value of the variable and initial and final values of $\dot{V}O_2$. Data from subjects whose cardiac output for an exercise level was more than two standard deviations from the age specific predicted values of Hossack et al. (1983) were excluded from the analysis. These outliers were associated with a predicted arterial PCO_2 that averaged 5.4 to 8.3 mmHg higher than the measured end-tidal PCO_2. The high predicted arterial PCO_2 value in these cases resulted in extremely high cardiac output values (average $\dot{Q}$ 20.3 l/min at a $\dot{V}O_2$ of 2.1 l/min). These values are outside of the physiological range for this age group. This result suggests that the Bradley equation does not accurately predict the arterial PCO_2 value in some of the elderly. However, alternate equations (Jones et al., 1979) resulted in more pronounced errors. Differences between groups were tested for each load (low, medium, and high submaximal levels) separately. This approach allowed us to retain data for each subject even if information was missing for one exercise intensity and allowed us to assess the change in a variable without

interpolating to a common oxygen uptake. This multivariate approach also permitted us to control the effect of other variables (e.g., body weight).

Results.

The physical and physiological characteristics of the control activity group members at baseline and final testing are presented in Table 15. No significant differences between the two groups were observed at baseline. We observed a decline in heart rate at each submaximal load between the initial and final tests in the activity group that was significant with respect to the control group (Figure 10). Maximum oxygen uptake was also significantly increased from T1 to T2 in the activity group with respect to the controls indicating that the exercise training program was an adequate stimulus to the cardiorespiratory system (Table 16). No change in maximum heart rate as a result of the training was observed. The incidence of angina fell from 7 to 5 occurrences in the activity group. No change was observed for control group members.

The relation between cardiac output and $\dot{V}O_2$ for both groups at T1 (baseline) and T2 (final) is displayed in Figure 11A. Note that the number of data points varies between loads. The full data set is plotted to facilitate comparison with the results of the multiple regression analysis. In all cases the pattern of change observed is very similar to that produced when an equal number of data points is plotted across exercise intensities. Differences in the pattern of change between plots

with equal and unequal n's are noted in the text. The trend toward increased $\dot{Q}$ at a given $\dot{V}O_2$ at T3 with respect to T1 was not statistically significant nor was there a significant difference between groups. This was also true for stroke volume (Figure 11B) and $CaO_2-C\bar{v}O_2$ (Figure 11C). The slope of the relation between $\dot{Q}$ and $\bar{V}O_2$ ranged between 5.1 and 5.4 which is within the range of values compiled by Faulkner et al. (1977) in their survey of the literature.

Stroke volume increased slightly from the low to medium submaximal loads (mean increase 3.5ml) in both groups at initial and final testing (Figure 11B). At baseline testing stroke volume fell in both groups from the second to third submaximal loads (average decrease 3.8ml). With unequal numbers of subjects at T1 and T3 and between loads it appears that training results in an increase in SV from the 2nd to 3rd load. However, with equal numbers of subjects it is apparent that both groups show an increase in SV from medium to high submaximal exercise loads at T2 (mean increase control group 1 ml, training group 1 ml). Those subjects who experienced angina or who had a previous myocardial infarction showed basically the same pattern with no change between the low and medium levels and a drop to the high load. The increase in arterio-venous oxygen content difference through low to high workloads reflects the balance between increasing cardiac output and $\dot{V}O_2$ (Figure 11C). No difference in systolic blood pressure response between activity and control groups was observed (Figure 11D). However, if the systolic blood pressure values for control and activity subjects are pooled a

TABLE 15. Subject description for activity and control group members at baseline testing. Values are means and (standard errors). No significant differences were observed in the baseline measures.

Variable	Activity	Control
Age (yrs)	62.3 (0.42)	62.4 (0.43)
Weight (kg)	77.8 (1.5)	80.3 (1.4)
FEV1.0 (l/sec)	2.82 (0.42)	2.83 (0.43)
$\dot{V}O_2$max (l/min)	2.30 (0.06)	2.34 (0.07)
MI (n)*	5	2
Angina (n)*	7	3

* Values are number of subjects i) who had a myocardial infarction (MI) before entering the study ii) who experienced angina during stress testing.

Figure 10. Relation between heart rate and oxygen uptake through three submaximal exercise levels in control (□) and activity (●) groups. Values for baseline (——) and final (— —) testing in both groups are illustrated. Number of values plotted at each point is as illustrated in Figure 11A.

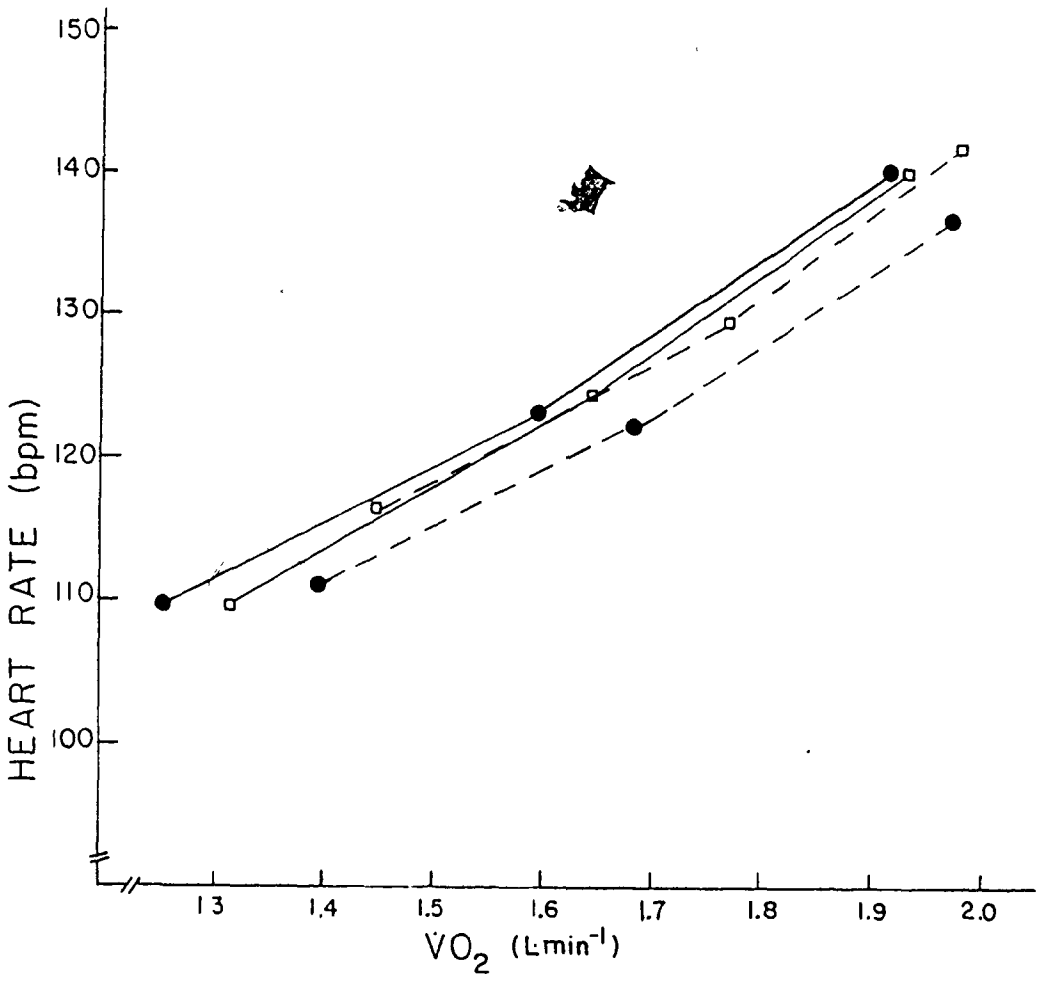


Figure 11 A,B,C,D,. Cardiovascular function during submaximal exercise at baseline and final testing in control and activity group members. Note varying sample size across loads at from T1 to T3. Figure 11A depicts the relation between cardiac output and oxygen uptake; 11B for stroke volume and $\dot{V}O_2$; 11C shows the increase in arterio-venous oxygen content difference ($CaO_2-C\bar{v}O_2$) with increasing exercise intensity; 11D depicts the increase in systolic blood pressure with increasing $\dot{V}O_2$ and the drop in blood pressure from T1 to T3.

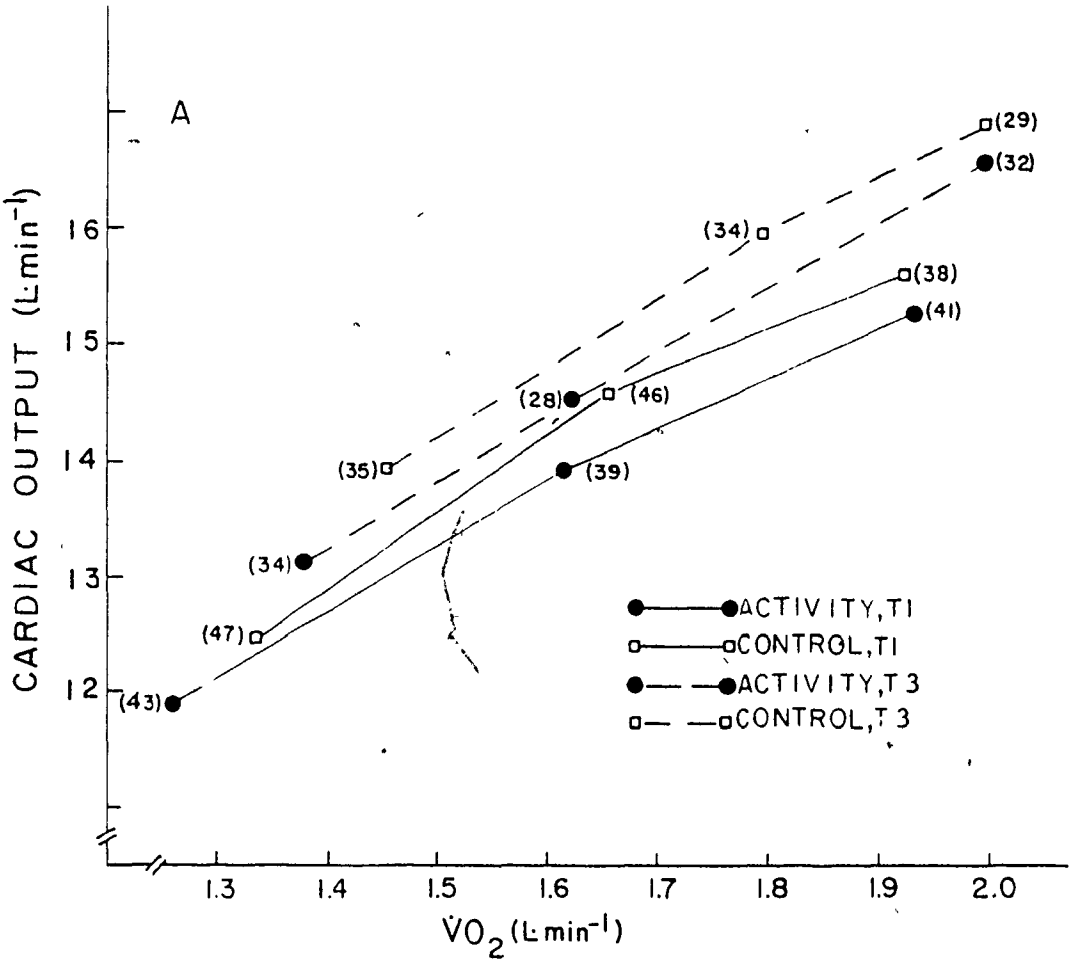


Figure 11B. Relation between stroke volume and oxygen uptake in control (C,□) and activity (A,●) groups.

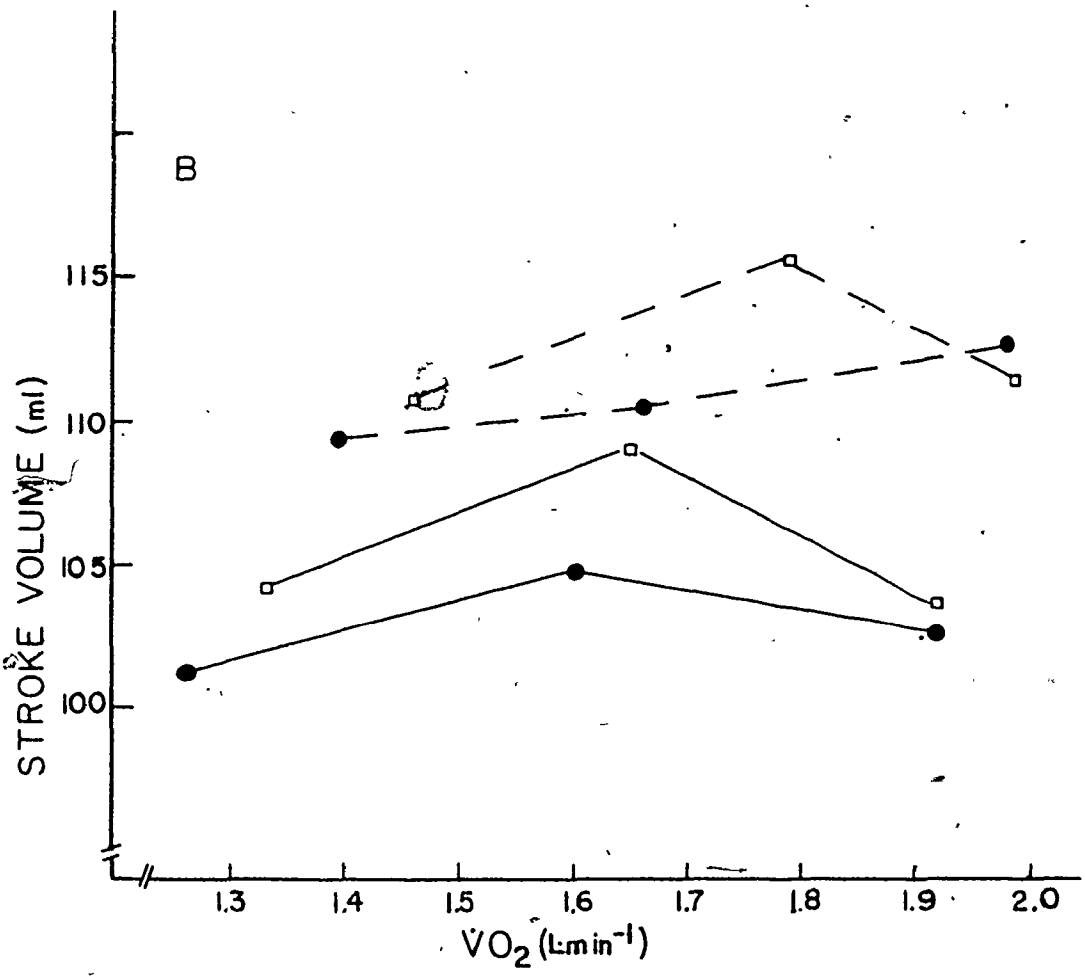


Figure 11C. Relation between $CaO_2-C\bar{v}O_2$ and oxygen uptake in control (C,□) and activity (A,●) groups.

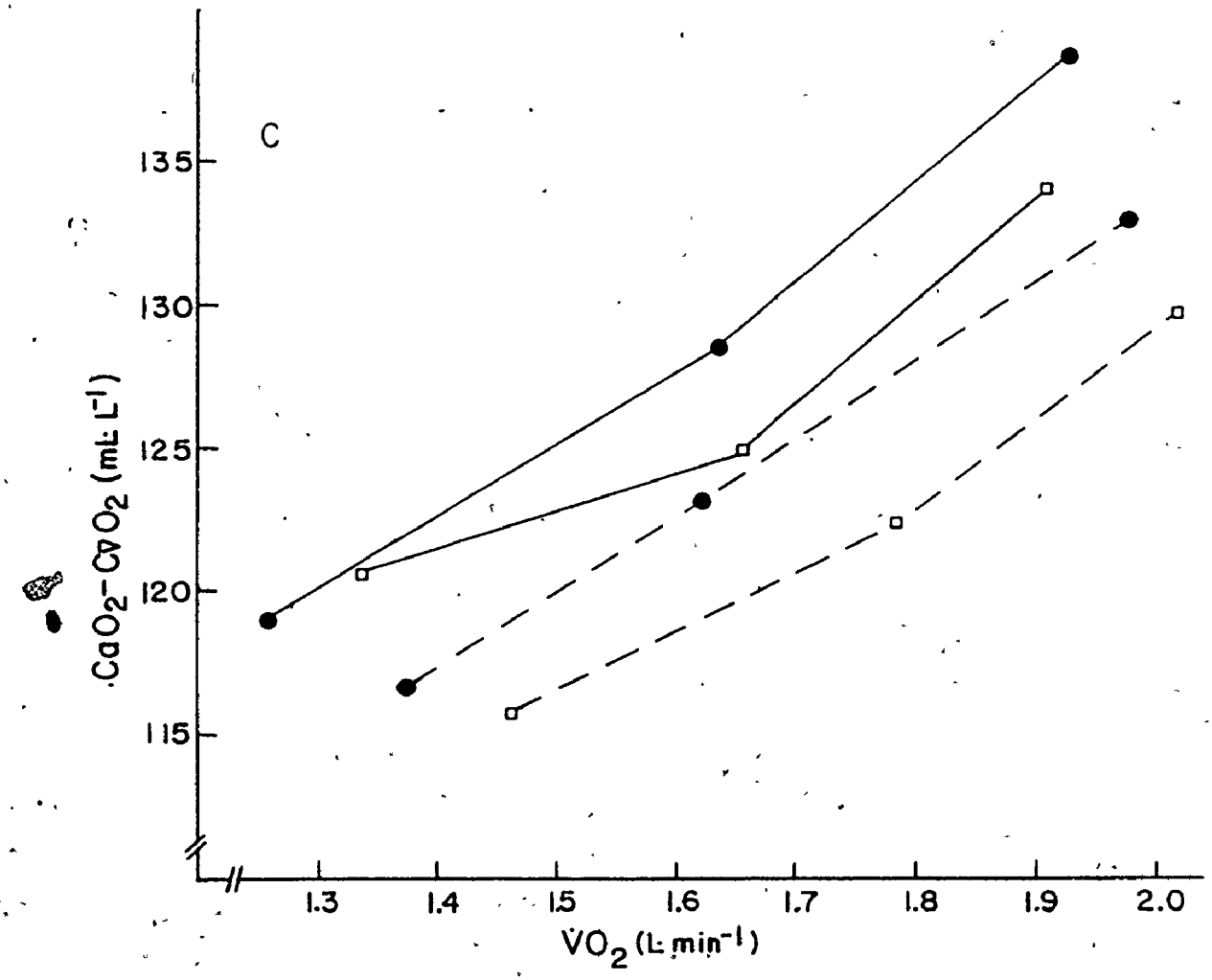


Figure 11D. Relation between systolic blood pressure and oxygen uptake in control (C,□) and activity (A,●) groups.

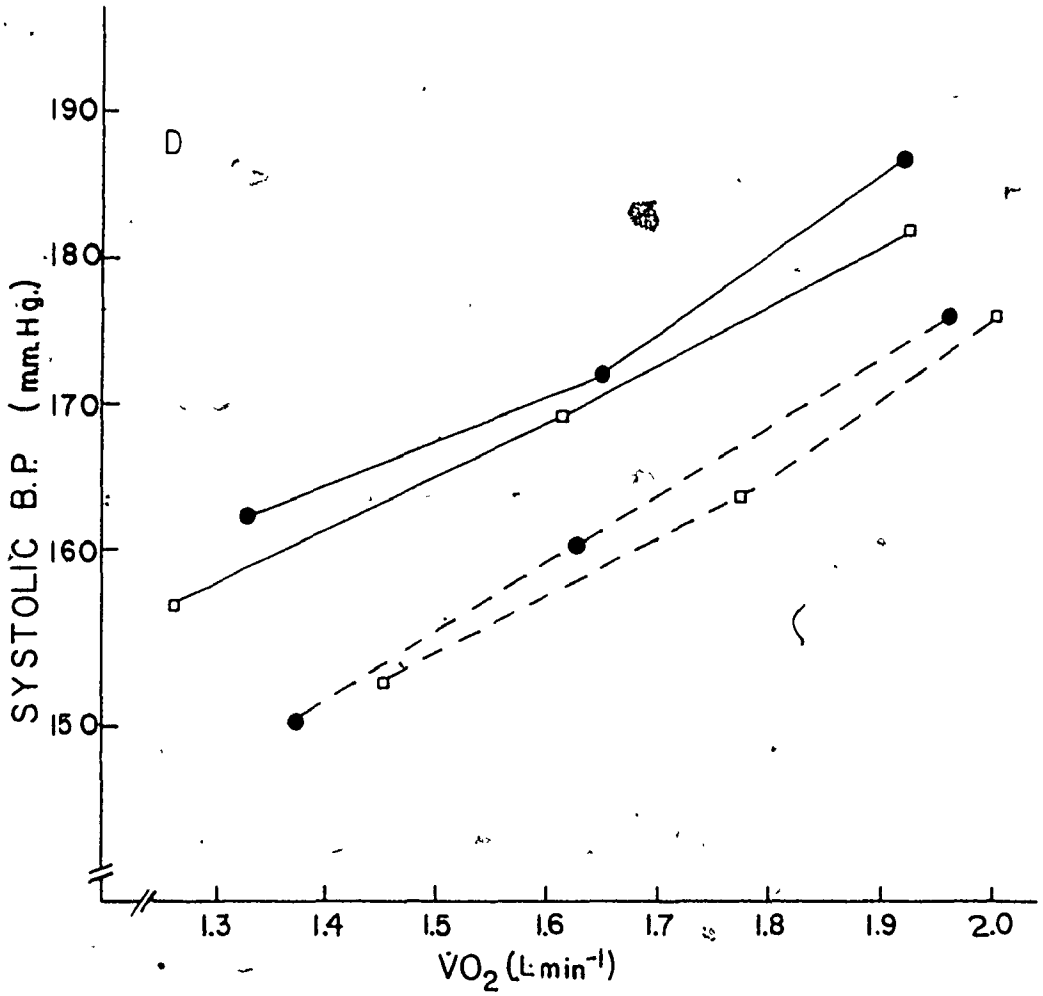


Table 16. Comparison of control and activity groups during maximal exercise at baseline (T1) and final testing (T2). Values are means (s.d.).

Variable	Activity (n=46)		Control (n=52)	
	T1	T2	T1	T2
HRmax	158 (2)	159 (2)	158 (2)	162 (2)
BPsys (mmHg)	182 (3)	181 (3)	187 (3)	183 (3)
$\dot{V}O_2max$ (l/min)	2.30 (0.06)	2.54* (0.08)	2.34 (0.07)	2.42 (0.07)
$\dot{V}Emax$ (l/min)	81.0 (3.2)	82.2 (3.3)	83.7 (3.3)	92.4 (4.1)
Weight (kg)	77.8 (1.5)	77.2 (1.5)	80.3 (1.4)	83.0 (1.5)

* difference between T1 and T2 is significantly greater in the activity versus control group ($p < 0.05$).

significant decrease ($p < 0.05$) in blood pressure at a given $\dot{V}O_2$ is observed. Rate - pressure product was also significantly reduced between T1 and T2 for the combined groups.

Discussion.

One year of exercise training produced the expected training bradycardia during submaximal exercise and an increase in maximal oxygen consumption but did not otherwise alter the cardiovascular functions which we measured. However, one year after retirement systolic blood pressure during exercise was significantly reduced in both the training and control groups. The mechanism(s) underlying this change are unknown. However, in response to a questionnaire, both groups of subjects indicated that they were experiencing less stress one year following retirement compared to shortly before retirement (Table 17). This was not reflected in a decrease in blood pressure at rest. The possibility that the decrease in systolic blood pressure was due to accomodation to treadmill testing exists but seems improbable since the subjects had been habituated to the treadmill and had performed one maximal test before the test in which these blood pressure measurements were made. Seals et al. (1984) observed a significant fall in mean blood pressure following light or high intensity training in their elderly subjects.

In young subjects endurance training of large muscle groups is associated with increases in both $CaO_2-C\bar{v}O_2$ and stroke volume (Rowell, 1974; Thomas et al., 1981). Our results indicate that changes in both $CaO_2-C\bar{v}O_2$ and stroke volume play a role in the response of elderly males to training. However neither of these variables changed significantly with respect to the control group suggesting that there is wide variation in the manner in which the adaptation to training is made.

Authors have reported differing findings concerning the relation between stroke volume or $CaO_2-C\bar{v}O_2$, and oxygen uptake during performance of dynamic exercise by elderly subjects (Becklake et al., 1965; Granath et al., 1964; Hartley et al., 1969; Julius et al., 1967; Niinimaa and Shephard, 1978; Seals et al., 1984). In contrast to findings reported by Horvath and Borgia (1984) for an 85 year old subject we found that the $CaO_2-C\bar{v}O_2$ difference widened with increasing exercise intensity. Our results of a small increase through moderate exercise and a levelling off or fall in stroke volume with heavy exercise are in agreement with the findings of several authors (Granath et al., 1964; Hartley et al., 1969; Seals et al., 1984). However, the change in stroke volume with increased exercise intensity was very small in all these studies. The conflicting result observed by Niinimaa and Shephard (1978) may have resulted from their estimation of arterial PCO_2 from end tidal PCO_2 using the empirical equation developed by Jones et al. (1979) using a group of young men. We computed

Table 17. Comparison of change in perceived stress from baseline testing (T1) to one year after retirement (T2) for the combined control and activity groups.

Change in stress over the past two years (% of group)	T1	T2
1) less	29.3	80.3
2) ~ same	57.7	16.8
3) more	13.0	2.9

cardiac output and dead space to tidal volume ratios with arterial PCO_2 values predicted from the Jones relation and found consistently low cardiac output values and negative dead space to tidal volume ratios in approximately 30% of the sample. The relation between end tidal and arterial PCO_2 is probably altered by aging related changes in the lung which result in increased dead space at rest and during exercise (Tenney and Miller, 1966) and greater inhomogenity in ventilation perfusion ratios. The Jones' equation therefore may not be applicable to an elderly population. The equation developed by Bradley et al. (1976) includes an age correction which increases the predicted dead space relative to that for a young subject. This is an empirical equation which we found adequate for the majority of observations. However, further study of the relation between arterial and end tidal PCO_2 values in the elderly is required to increase the precision of the prediction.

The slope of the relation between cardiac output and $\dot{V}O_2$ observed in this study was similar to that cited by Faulkner et al. (1977). The average $\dot{Q}$-$\dot{V}O_2$ intercept (ml/kg·min) for our subjects was approximately 60 at baseline and 65 one year later. Faulkner and his colleagues (1977) on the basis of their review of literature suggest an intercept of 49 ml/kg/min for sedentary men over age 40 and an intercept of 66 for the physically active of any age. Exercise training did not affect the slope or intercept of the relation between $\dot{Q}$ and $\dot{V}O_2$ in this study in agreement with the conclusions of Faulkner et al. (1977). Schocken et

(1977). Schocken et al. (1983) in contrast, using radionuclide angiocardiography observed an increase in cardiac index following exercise training of elderly (mean age 72 yrs.) men and women.

The capacity of the cardiovascular system to adapt to exercise is diminished with increased age (Gerstenblith et al., 1976). Maximal stroke volume and cardiac output are reduced in the elderly. Gerstenblith et al. (1976) have suggested that increased impedance to ejection may limit the ability of the elderly to augment stroke volume. Decreased impedance to ejection would result from the fall in systolic blood pressure observed over the year in our subjects and may underlie the non-significant increase in cardiac output and stroke volume observed in both the control and activity groups. However, cardiac function during maximal exercise is not affected since maximal systolic blood pressure was not altered in either group and $\dot{V}O_2max$ increased only in the activity group. We did not calculate mean arterial blood pressure since difficulties with treadmill noise and arm movement reduced the reliability of our diastolic blood pressure measurements.

In summary, it appears that there is not a common pattern of adaptation to a training stimulus in the elderly since non-significant changes in both $Ca0_2-C\bar{v}0_2$ and stroke volume were observed. A reduction in systolic blood pressure during dynamic exercise was observed which was not related to participation in a program of endurance training. The pattern of change in stroke volume was not

affected by participation in endurance training.

4.6 Pulmonary factors and $\dot{V}O_2max$

Introduction.

The observation that FEV1.0 is correlated with $\dot{V}O_2max$ suggests that pulmonary function may influence the capacity of the elderly to perform dynamic exercise. Large declines in pulmonary function relative to other components of the gas transport system are observed with aging. While the decline in maximal oxygen uptake ($\dot{V}O_2max$) is approximately 40 % between the third and seventh decades of life the decrease in maximal breathing capacity is 60 % (Skinner, 1971). This decline in pulmonary function markedly reduces the ventilatory reserve available to the elderly. While some authors have dismissed (Bruce, 1984) and others have suggested (Skinner, 1971) a possible ventilatory limit to oxygen uptake it appears that this possibility has recieved little study (Dubois et al., 1979).

Using data from a large sample of elderly men from both before and after one year of endurance training we address three issues; 1) whether ventilation limits maximal exercise performance in the elderly; 2) whether ventilatory reserve is altered as a result of endurance training by elderly subjects and finally; 3) whether the beneficial effects derived from training vary with the lung function of the subjects.

Methods.

Subjects.

Men who were retiring from their occupations were contacted as described in the general methods section (Chapter 3.1). The one hundred and forty five men who are examined in this section were tested using both the Stage I and Stage II tests. The subjects who were assigned to the activity group participated in a program of endurance training which involved thirty minutes of walking or jogging at a prescribed heart rate three mornings per week for one year. Further details of the training program and results are available elsewhere (Chapter 3.4).

Data Collection.

At baseline and one year later anthropometric and physiological measures were made over three visits to the laboratory. Resting pulmonary function was determined from the highest values of three trials for vital capacity (VC), forced expiratory volume in one second (FEV1.0), and maximum mid-expiratory flow rate (MMEFR). Maximal stress tests were performed by each subject on their second (Stage I) and third (Stage II) visits to the laboratory. Fifty six subjects completed one year of training and underwent a Stage II test at the end of the year of training.

Data Analysis.

Several derived measures were calculated. Cotes (1979) has suggested that when the ratio of tidal volume (VT) to vital capacity (VC) exceeds 55 to 60% dyspnea will ensue. The VT/VC ratio for the final three

minutes of the Stage II test was calculated to evaluate the possibility that dyspnea occurred. Cotes (1979) also suggests calculating the ratio exercise ventilation to directly determined or estimated maximal breathing capacity to assess the ventilatory response to exercise. The indirect maximal breathing capacity (IDMBC) was estimated from the forced expiratory volume (Cotes, 1979; McKerrow et al., 1960). The ratio of VEmax to IDMBC gives a rough estimate of the proportion of the ventilatory reserve which the subject is using to meet the gas exchange demands of exercise.

The data were also analyzed by dividing the sample into two groups; those with FEV1.0 values in the lower 40% versus the upper 40% of the range of FEV1.0 values found in this study. The maxima ($\dot{V}O_2$, $\dot{V}E$, HR) achieved by subjects with FEV1.0 values in the lower 40% (low FEV group) of the range observed in this study were compared with the maximal values reached by subjects whose FEV1.0 measure fell in the upper 40% (high FEV group) of the sample. Multiple regression analysis was used to test the hypothesis that the response to training would be less for the low FEV versus high FEV group. The ratio of maximum minute ventilation to $\dot{V}O_2$max ($\dot{V}E$max/$\dot{V}O_2$max) was calculated for the test where the highest oxygen uptake was achieved.

Results.

The resting pulmonary function of subjects in this study is within one standard deviation of the mean values predicted from regression equations published for this age group (Cotes, 1979, p. 369)(Table 18).

Tidal volume and breathing frequency measures at baseline reached 90% of their maximal value 3 minutes before the end of a maximal Stage II treadmill test. The tidal volume was greater than 60% of vital capacity during the final three minutes of the baseline test and $\dot{V}E$max was almost 80% of the indirect maximum breathing capacity (Table 19). The range of values for $\dot{V}E$max/IDMBC exceeded 100% (44 to 134%). The ventilatory equivalent for oxygen during maximal exercise was slightly higher than the values observed with young adults (Astrand and Rodahl, 1977).

The effect of training on pulmonary function, the maximum values for $\dot{V}O_2$, $\dot{V}E$, and heart rate and on the ratios used to illustrate the interaction between resting pulmonary function measures and ventilation during exercise is displayed in Table 19. The increase in average $\dot{V}O_2$max from baseline to final testing for the training group was 10.4%. The $\dot{V}O_2$max after one year was significantly greater for the training group with respect to the control group after controlling for differences in the initial value through multiple regression. The

Table 18. Description of the subject sample. Physical characteristics and measurements of pulmonary function made at rest. (n = 145).

Variable	Mean	Range		Standard Deviation
		Minimum	Maximum	
Age (yrs)	62.4	55.0	68.0	3.0
Weight (kg)	78.8	57.0	111.3	10.6
Height (cm)	173.2	153.4	196.4	6.9
FVC (l)	3.80	2.20	6.00	0.67
$FEV_{1.0}$ (l/sec)	2.82	1.50	4.26	0.52
$FEV_{1.0}/VC$ (%)	74.6	34.8	100.0	8.1

Table 19. Pulmonary function during maximal exercise in elderly males. Values for control (C)(52) and activity (A)(46) group members are tabulated for baseline and final tests. VO_2max is given in ml/kg·min. Probability levels indicated are between baseline and final (T2) testing in Control and Activity groups.

Variable	Group	Initial	Final	Mean Diff.	p value
VO_2max	A	30.7	33.9	3.2	0.001
	C	29.1	30.2	1.1	0.072
VEmax	A	83.2	92.3	9.2	0.001
(l/min)	C	85.8	90.9	5.1	0.001
VEmax/VO_2max	A	35.4	35.9	0.5	0.357
	C	35.8	36.7	1.0	0.248
VEmax/IDMBC	A	81.7	89.4	7.7	0.001
(%)	C	82.4	87.7	5.3	0.102
VTmax	A	2.42	2.48	0.05	0.286
(l)	C	2.44	2.49	0.05	0.598
VTmax/VC	A	63.9	64.6	0.6	0.669
(%)	C	64.0	66.8	2.7	0.107
Freq. Bre.	A	34.4	37.9	3.5	0.001
(bre./min)	C	35.5	37.1	1.6	0.110

$\dot{V}O_2$max of the control group members did not change significantly over the year. A paired t-test indicated that the increase in maximum minute ventilation from base line to final testing was significant for both groups ($p < 0.001$). The magnitude of the increase was significantly greater in the activity group. The ratio of VEmax to predicted maximal ventilation sustainable for 4 minutes was higher after training for the exercise group (11.0% increase), and with respect to the control group. There was no significant change in FEV1.0, VC or MMEFR for either the control or exercise group from baseline to final testing.

Subjects whose FEV1.0 fell in the bottom 40% (mean FEV1.0=2.32 l/sec) of the range for this sample of elderly men had significantly lower $\dot{V}O_2$max and maximum minute ventilation values compared to subjects with FEV1.0 values in the upper 40% (mean FEV1.0=3.32 l/sec) of the sample (Figure 12A, 12B). This was not due to a common relation of FEV1.0 and $\dot{V}O_2$max or VEmax with body size because FEV1.0 and $\dot{V}O_2$max continued to be significantly associated when the influence of weight and height was controlled through multiple regression analysis. The proportion of smokers was approximately equal in the low FEV group and the high FEV groups. The effect of training on the group with low FEV1.0 values was significantly less than for the subjects in the upper range of FEV1.0 values. The increases in $\dot{V}O_2$max and VEmax were 30% and 15% larger in the high FEV1.0 group compared to the change observed in the low FEV1.0 group (Figure 12A, 12B). Maximum heart rates did not differ significantly between groups or with training ($p>0.05$)(Figure 12C).

Figure 12 A,B,C. The effect of pulmonary function ($FEV_{1.0}$) on 1) the response to maximal exercise 2) the response to one year of training. Subjects are grouped according to activity (control, CONT or activity, ACT) and pulmonary function (CONT-LOW, control group subjects with $FEV_{1.0}$ in lower 40% of the sample; CONT-HIGH, control group with $FEV_{1.0}$ in upper 40%; ACT-LOW, ACT-HIGH activity group members with low and high $FEV_{1.0}$ values respectively.

Figure 12A. $\dot{V}O_2max$ before and after training in subjects with high and low $FEV_{1.0}$ values.

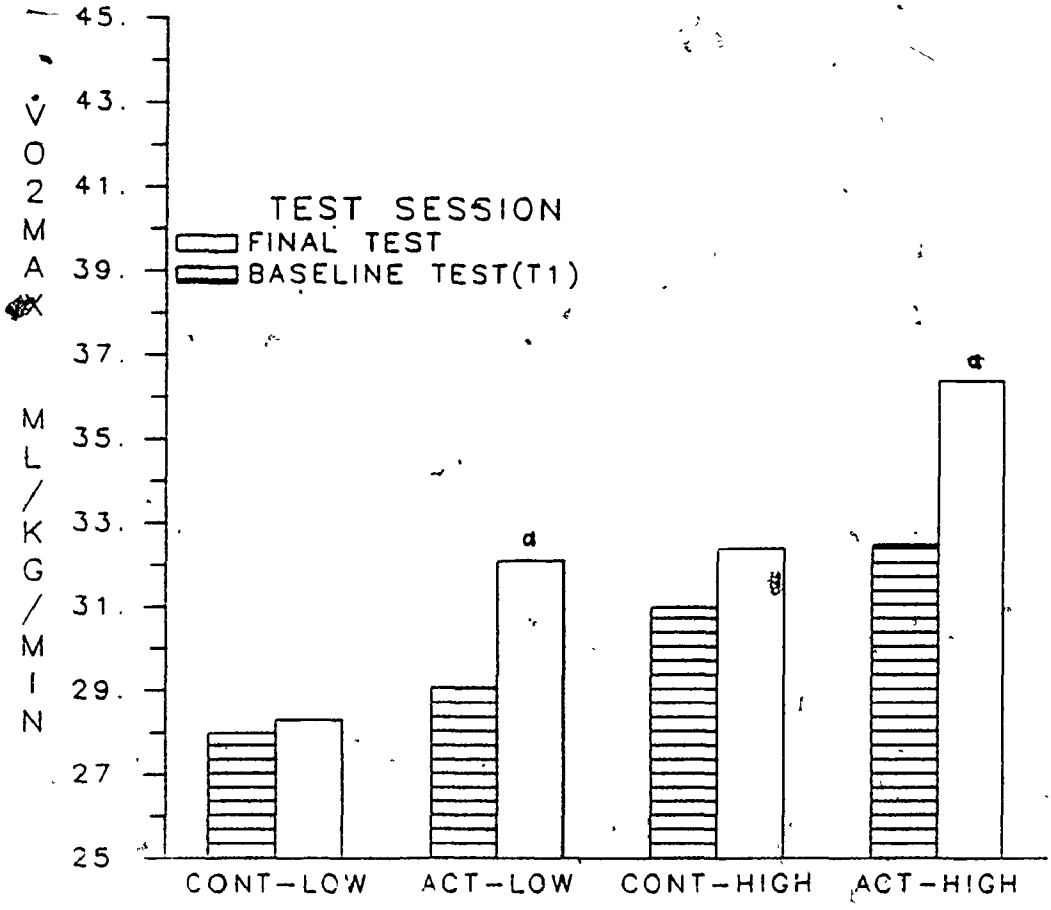


Figure 12B. Effect of pulmonary function on maximal ventilation in control and activity groups, before and after training.

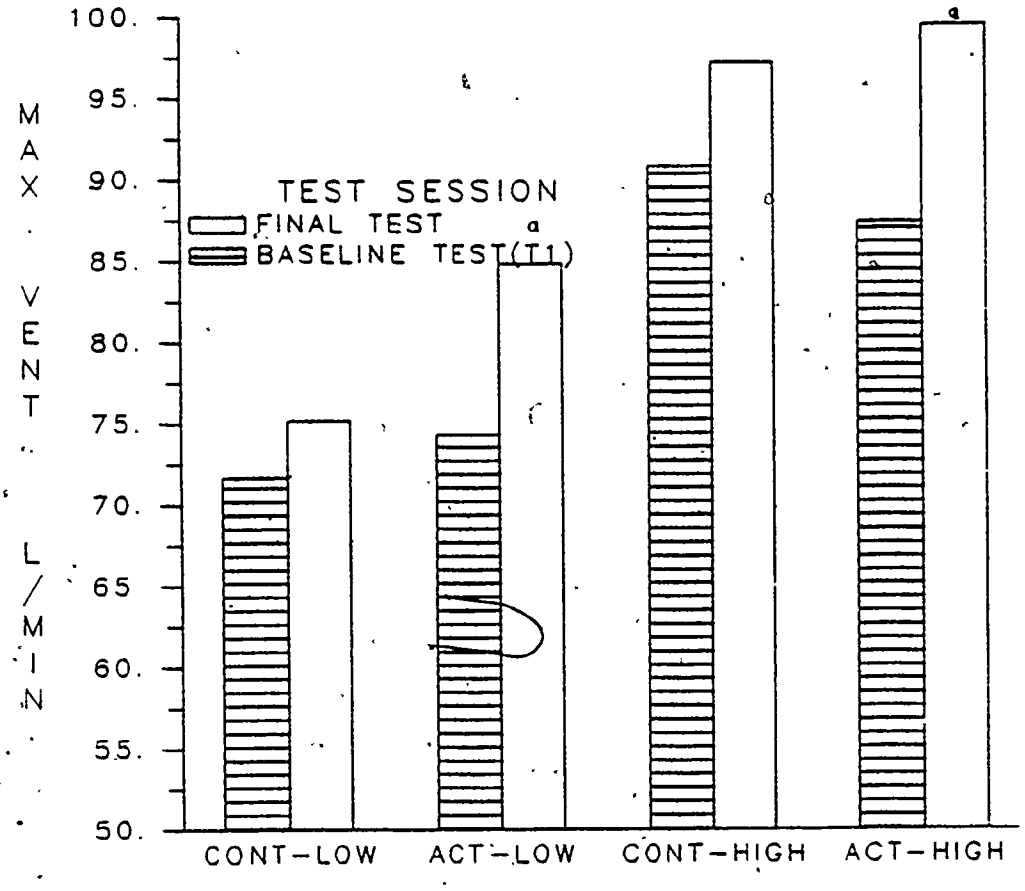
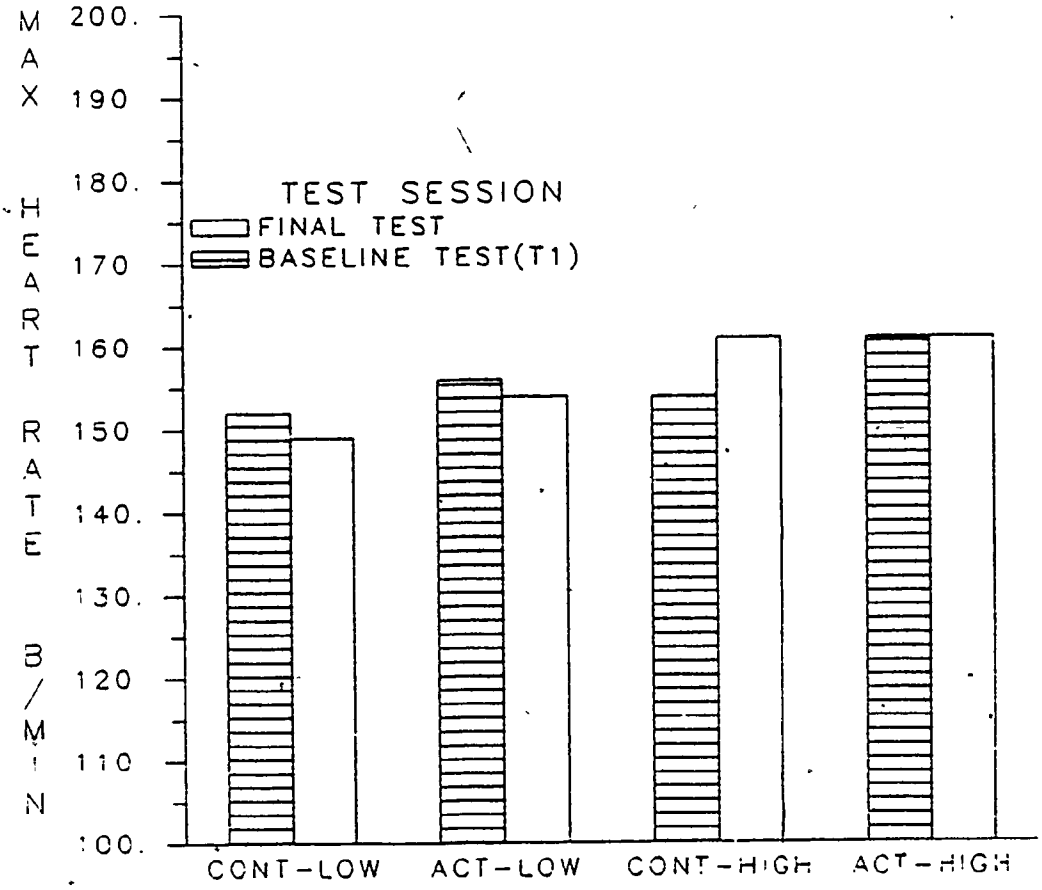


Figure 12C. Effect of pulmonary function on maximal heart rate in control and activity groups, before and after training.



Discussion.

Routine measures of minute ventilation, and tidal volume during exercise and simple spirometric measures such as FEV1.0 indicate that some elderly subjects do approach the limits of their ventilatory capacity during maximal stress testing on a motor-driven treadmill. Furthermore the ventilatory reserve is reduced following endurance training; presumably because the capacity of the other components of the gas transport system is increased while the ventilatory system is not significantly affected. Our third major finding is that those individuals who have impaired lung function appear to benefit less from a walk/jog program of aerobic exercise than those with normal function.

Szekely et al.° (1982) found that young (19-31 yrs) subjects continued to increase tidal volume through to the end of maximal exercise. In contrast, Lind and Hesser (1984) have reported that in young subjects tidal volume plateaus at about 2.4 liters, or 46% of vital capacity. The tidal volume of the elderly subjects in the present study increased very little over the last 3 minutes of maximal exercise and plateaued at 2.40 liters which represents more than 60% of the reduced vital capacity of these elderly subjects. DeVries and Adams (1972) found that during submaximal exercise the elderly (mean age 69.2 yrs) reached a plateau in tidal volume when minute volume was approximately 40 liters per minute. The near constancy of tidal volume

and the high proportion of vital capacity (60%) used during the final minutes of a progressive test to maximum suggests that, possibly because of dyspnea, tidal volume could not be increased further. Increases in ventilation therefore could only be achieved through increasing breathing frequency. An increase in breathing frequency requires an increase in ventilatory flow rate to maintain tidal volume. With a breathing frequency of 37 and assuming that expiration requires 60% of the total breath duration the time available for expiration is 0.96 seconds. With an average tidal volume of 2.48 liters the expiratory flow will be 2.6 liter/sec or greater than 90% of FEV1.0. The significant correlation between $\dot{V}O_2$ and FEV1.0 may arise because the requirement for increased flow impinges on the maximum expiratory flow rate which is decreased because of loss of elastic recoil (Klocke, 1977). The impact of smoking on $\dot{V}O_2$ max was small and apparently through its association with reduced FEV1.0 values.

The ratio of $\dot{V}E$max to maximal voluntary ventilation (MVV) or to IDMBC is typically 65 to 70% in young non-athletic subjects and may reach 91% in endurance athletes (Mahler et al., 1981). The elderly men in this study used a large proportion (81%) of their ventilatory reserve during the baseline testing. Those subjects who completed one year of endurance training were even closer to the limit of their predicted capacity (89%). This confirms the observation (Chapter 4.3) made in a smaller group of men who attained greater than 90% of their MVV during maximum exercise on a cycle ergometer. In elite athletes it appears that training may improve the function of the gas transport system to the

point where ventilatory function limits exercise performance. Air flows which encroach on the maximal flow-volume envelope have been observed during maximal exercise performance by athletes (Grimby et al., 1971). In the elderly the ventilatory reserve before training is small enough so that an increase in demand for ventilation required by the increase in maximal $\dot{V}O_2$ and $\dot{V}CO_2$ may exceed their capacity.

The present findings indicate that exercise performance in the elderly may be limited by ventilatory factors but do not address what the physiological mechanisms underlying the limit might be. Inadequate ventilation will result in arterial hypoxemia and inadequate respiratory compensation for exercise induced metabolic acidosis. Arterial hypoxemia and decreased arterial pH during performance of maximal exercise by athletes has been observed (Dempsey et al., 1984; Rowell et al., 1964). Observations on elderly subjects during maximal exercise have not been made. Decreased efficiency of breathing due to increased dead space ventilation (Tenney and Miller, 1966), increased difference between alveolar and arterial oxygen partial pressures (Muiesen et al., 1971) and less homogenous distribution of ventilation (Cotes, 1979, p383) predispose the elderly to reaching a ventilatory limit to gas exchange. The increased ventilatory equivalent for oxygen observed during maximal exercise by our elderly subjects suggests less efficient gas exchange. The probability of respiratory fatigue is increased because of the increased work of breathing (Turner et al., 1968) and decreased respiratory muscle strength (Black and Hyatt, 1969) observed in the

elderly. Ventilatory muscle training may reduce the incidence of respiratory muscle fatigue (Leith and Bradley, 1976) but the effect of endurance training on ventilatory muscle performance in the elderly has not been studied. We did not make measures such as respiratory muscle strength or maximum inspiratory flow rates which would reflect such an improvement. Training did not influence those pulmonary functions which were measured in this study (FEV1.0, MMEFR, and VC) which are determined largely by the mechanical properties of the lung (Hyatt, 1983).

The smaller training response of subjects with low FEV1.0 values might be attributed to a common relation of FEV1.0 and training response to another factor which would directly affect the response to physical training. We evaluated this possibility by examining the correlation of FEV1.0 with factors which might be expected to influence the magnitude of the training response such as training intensity and frequency. The correlations between FEV1.0 and these two variables were very low ($r<0.1$) and not significant. A positive correlation ($r=0.33$, $p<0.001$) between FEV1.0 and $\dot{V}O_2$max at entry to the study was observed. The low initial $\dot{V}O_2$max values found in subjects with low forced expiratory volumes should predispose them to a large training response where as we found that these subjects demonstrated a smaller increase in $\dot{V}O_2$max with training. This suggests that low forced expiratory volume exerts an independent effect on the ability to benefit from training in the elderly.

CHAPTER FIVE
GENERAL CONCLUSIONS

Aging reduces the ability to perform endurance activity. This is reflected in an age related fall in maximum oxygen uptake, ventilation threshold and rate of response to increased exercise intensity. $\dot{V}O_2max$ is a valuable indicator of aerobic capacity and can be reliably and reproducibly measured in the elderly. However, submaximal exercise performance is also related to the ventilation threshold, and rate of response and these measures can be assessed in the same test protocol. The maximum oxygen uptake of elderly males can be increased in response to a training stimulus. This finding has important implications for the health of older members of society. Their ability to function independently may be augmented by regular exercise training. However, the maximal oxygen uptake of an elderly subject and the amount of increase observed with training are quite variable and our ability to predict either is limited. The factors which are strongly correlated with training response in young adults are not good predictors in the elderly. The presence of cardiovascular disease, as indicated by the reason for halting an exercise test, appears to limit the effectiveness of physical training in the elderly male. The nature of the physiological adaptations which underlie the response to training is ill defined. The role of the cardiovascular system in the response to

physiological adaptations which underlie the response to training is ill defined. The role of the cardiovascular system in the response to training requires further study to define what determines whether an elderly subject adapts by increasing stroke volume, by increasing the amount of blood shunted to the muscles, by increasing the extraction of oxygen by the working muscles or by a combination of these mechanisms. Improvements in our ability to non-invasively assess cardiac output during exercise are required to make precise measures in large numbers of subjects. The ability to effect increases in the ventilation threshold relative to $\dot{V}O_2max$ with moderate intensity physical training of elderly subjects is quite limited. The pulmonary system appears to play a more important role in determining exercise capacity in the elderly than is reported for young adults. The ventilatory reserve during maximal exercise is very small in elderly men and the response to endurance training appears to be impaired by poor pulmonary function.

The conclusions from this thesis are: 1) that $\dot{V}O_2max$ can be measured reliably in the elderly but that a minimum of two tests are required to obtain a good measure;

2) the elderly respond strongly to a training stimulus. The mean $\dot{V}O_2max$ increase observed in those subjects who complied with the program was 12%;

3) the magnitude of the response is variable and is not strongly related to exercise training intensity but may relate to the presence of pathology. The weak association between training intensity and response

is in marked contrast to what is observed with young adults and deserves further study. This finding is of practical importance since it suggests that the elderly need not exercise at intensities which might produce orthopaedic or cardiovascular injury in order to improve $\dot{V}O_2max$;

4) pulmonary reserve is markedly reduced in the elderly and pulmonary function may limit performance in some of the elderly. In addition physical training further reduces the pulmonary reserve of the elderly. After training the elderly may be more prone to a ventilatory limit. The mechanism by which ventilation is limiting was not explored in this thesis;

5) the effects of training on the cardiovascular system are extremely variable. Accurate determination of cardiac output in the elderly by the non-invasive Fick method for CO_2 may be limited by the ability to estimate $PaCO_2$. Further studies to define the relationship between Pa and PET CO_2 are required.

6) ventilation threshold is elevated relative to $\dot{V}O_2max$ in the elderly and is not markedly influenced by training.

7) the rate of response (t1/2) to changes in exercise intensity is reduced in the elderly.

A recurrent problem in studying the elderly was the large variations in baseline values and responses to training. This large variablity is probably related to differing life histories. In a study with a large sample size, such as the one this thesis is based on, the variation in baseline measures can be dealt with by using a multivariate

analysis approach which employs the baseline value as one of the variables.

APPENDIX A
GLOSSARY OF TERMS AND ABBREVIATIONS

A-a	difference between alveolar (A) and arterial (a) pressures of a substance
aerobic	in the presence of oxygen
ATPase	enzyme which catalyzes the energy releasing removal of one phosphate from adenosine triphosphate (ATP)
$a-\bar{v}O_2$	difference in oxygen content between arterial and mixed venous blood (ml O2/liter of blood).
B-blockage	use of a drug (e.g., propranolol) to inhibit stimulation of receptors which would cause increased heart rate.
BTPS	body temperature (310 K) and pressure saturated, the volume of gas ventilation is corrected to these conditions
DL,CO	diffusing capacity of the lung for carbon monoxide.
FEV1.0	forced expiratory volume, volume of air which can be expired in the first second of expiration from vital capacity
Hb	haemoglobin (grams/deciliter)
HR	heart rate (beats per minute)
IDMBC	indirect maximal breathing capacity.
MET	unit of energy expenditure equal to oxygen consumption of 3.5 ml/kg/min. Approximates the resting METabolic rate.
MMEFR	maximum mid-expiratory flow rate (l/sec)

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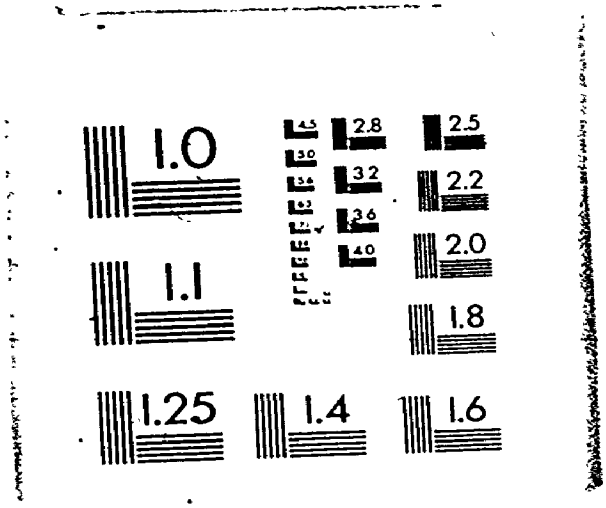


MRT	Mean Response Time (sec) time required to reach one half of final response, includes any time delay between stimulus and start of response.
PO.1	pressure generated at the mouth during the first 100 msec of inspiration (mmHg)
$\dot{Q}$	cardiac output - volume of blood ejected by the heart in one minute (liters/minute)
RER	respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$)
s.d.	standard deviation
SE	standard error of the mean
STPD	standard temperature (273 K) and pressure (760 mmHg) dry, gas exchange volumes are corrected to these standard conditions
Ti	duration of inspiration (sec)
t1/2	time required to reach one half of the final response magnitude
VC	vital capacity (l)
VE	volume expired in one minute
$\dot{V}/\dot{Q}$	ratio of lung ventilation to pulmonary blood flow
$\dot{V}O_{2max}$	maximum amount of oxygen the organism can consume in physical activity (liters/minute or ml/kg body weight/minute)
Vt	volume of one breath (l)

APPENDIX B

INFORMED CONSENT FORM

I agree to participate in a trial that will compare the effects of two different forms of activity on individuals following retirement. One group will take part in a program of graduated exercises that will include calisthenics and walking and/or jogging. The second group will not be part of a formal group but will carry on with their own activities as they wish. I understand that I will be put in one of the two groups depending on selection by lot.

I further agree to a preliminary medical examination that will include a detailed history and a clinical examination, simple measurements of height, weight, skinfold thickness and muscle strength, and electrocardiogram at rest and during graded exercise, the masurement of lung volumes (blowing into a small gasometer), the collection of respired gas during exercise (use of a mouth piece and nose clip) and the collection of samples of venous blood.

I understand that my progress will be assessed from time to time by simple exercise tests.

I an aware that while available evidence suggests that regular activity is beneficial, that there is a slight risk that a heart attack may be induced by physical activity.

The study will last approximately one year after the initial testing but I understand that I may withdraw from the study at any time.

WITNESS _____ SIGNED _____

DATE _____

APPENDIX C

EQUIPMENT AND METHODS

Breath-by-breath gas exchange.

The equations used to calculate gas exchange are based on those published by Beaver and his colleagues (1981). They were implemented in Fortran on a Digital Equipment Corporation mini-computer (MINC-11) which was designed for laboratory use. Inspired and expired ventilation were measured with a turbine device (Ventilation Measurement Module, Alphatech) which produces analog signals which are proportional to volume. Gas fractions were continously monitored using an electrochemical fuel cell analyzer for oxygen and an infrared analyzer for carbon dioxide. The oxygen analyzer contains a solid electrolyte which is highly conductive to oxygen ions. A difference in oxygen concentration between cathode (reference) and anode (sample) generates an electromotive force. The response time of the analyzer is approximately 0.2 s. Absorption of infrared light by CO2 reduces the amount of energy available to heat gas. Light from an infrared source is split and one beam is directed through the sample and the other through a reference cell. The difference in available energy is detected by heating gas with the light on either side of a thin metal diaphragm. The pressure difference generated distorts the membrane which is one arm of a Wheatstone bridge (Kamon, 1974). This generates an electrical signal which is proportional to the difference in CO2

concentration between the reference and sample gases.

The relations between gas fraction and voltage were determined before each test using three known gas mixtures. Delays for each gas between detection of flow and measurement of the gas fraction in that flow result from the physical arrangement of the measurement system and the response times of the gas analyzers. The response times in our measurement system were determined by measuring the time from onset of flow to 90% of the full response of each analyzer to a step change from room air to a gas mixture. The calibration routine also included logging the ambient temperature, barometric pressure and relative humidity into the computer file for correction of volumes to standard conditions.

Signals generated during both calibration and testing of subjects were sampled at 20Hz and the raw data was stored on disk for subsequent analysis. Initial data manipulation was possible on the mini-computer but final calculation of gas exchange required use of data arrays which were too large for the capacity of the laboratory computer. Data was transferred to a larger system available in the Natural Sciences Computing Center. Following these computations the responses (ventilation, $\dot{V}O_2$, $\dot{V}CO_2$, heart rate, respiratory exchange ratio, components of the breathing cycle) were graphed with the aid of a program developed for the laboratory computer.

The breath-by-breath measurement of gas exchange is based on measuring the volume of each gas inspired and expired. The basic equation

$$V_x = F_x\text{inspVIdt} - F_x\text{expVEdt}$$

is implemented for each gas ($x=CO_2$, O_2, N_2) using an approximation to integration based on the computer sampling rate (r = 20/sec)

$$(1/r) \cdot \sum_{n=1}^{N} (F_x\text{insp})_n (VI)_n$$

where N is the number of samples taken during inspiration. Expiratory volumes are dealt with in an analogous manner. With the turbine system the signal is proportional to volume rather than flow. Flow is calculated as the difference in volume between two samples. The concentrations signals are delayed in time with respect to the volume signal and must be aligned before integration is performed. This is accomplished by shifting the data in an array by the time delay measured in the calibration routine.

Cardiac output determination.

Cardiac output was estimated by applying the Fick equation to CO_2 exchange. The basic equation is

$$\dot{Q} = \dot{V}CO_2 / C\bar{v}-aCO_2$$

$\dot{V}CO_2$ is determined from the mixed expired gas fraction and expired gas volume

$$\dot{V}CO_2 = FeCO_2 \text{ X } VE,$$

The fractional pressure of venous CO_2 is estimated using the Collier method in which the subject rebreathes from a bag containing a high percent of CO_2 (9-20%). Mixing of gas between the alveoli and bag eventually (within 6 to 12 sec) results in an equilibrium of CO_2 concentration between the gas in the bag and the alveoli. The concentration of CO_2 in the alveoli is representative (with a small correction) of the concentration of CO_2 found in mixed venous blood. The empirical correction was developed by Jones et al. (1969)

$$P\bar{v}CO_2 = PbagCO_2 - [(0.24PbagCO_2) - 11mmHg]$$

Arterial CO_2 ($PaCO_2$) is estimated using the Bohr equation

$$PaCO_2 = PeCO_2/[1-(Vd+Vdappartus)/Vt]$$

where $PeCO_2$ is the pressure of CO_2 in mixed expired gas, Vdapparatus is the dead space of the apparatus and Vd is the physiological dead space. Physiological dead space is estimated from the equation developed by Bradely and her associates

$$Vd = 0.8698(age) - 1.29(height) - 0.4509(\dot{V}CO2) + 20.02(\dot{V}E) + 1291/(breathing\ frequency) + 270.4$$

where age is given in years, height in cm, $\dot{V}CO2$ in ml/min, $\dot{V}E$ in liters/min, and breathing frequency in breaths/min. The equation is empirically derived from studies with subjects through a broad range of ages (20-70 yrs).

Both the arterial and venous gas pressures must be converted to an amount in the blood (content, C). This requires an equation which incorporates the effect of the dissociation curve between haemoglobin

and CO_2. The relation developed by McHardy and modified by Jones (Paterson and Cunningham, 1976) was used.

ln(Content CO_2) = 0.396 X ln(PCO2) = 2.4. This relation assumes a haemoglobin content of 15 gm/dl and complete saturation of Hb with 02. The result must be corrected for individual deviations from these values.

$C\bar{v}\text{-}aCO_2 = C\bar{v}\text{-}aCO_2 - [15\text{-}Hb) \times 0.15 \times (P\bar{v}CO_2 - PaCO_2$

$C\bar{v}\text{-}aCO_2 = C\bar{v}\text{-}aCO_2 - [(100 - SaO_2) \times 0.064]$

where SaO_2 is the saturation of Hb with oxygen.

Hb was measured for each subject but a saturation of 95% was assumed. The magnitude of the error due to deviations from this value is very small.

Training Intensity Equation.

Training intensity was calculated with the following equation from Cunningham et al. (1974).

Training Intensity (METs) = 60 + max METs)(Max Mets)/100

where one MET is equal to 3.5 ml/kg/min of oxygen consumption.

Electrocardiographic Signs.

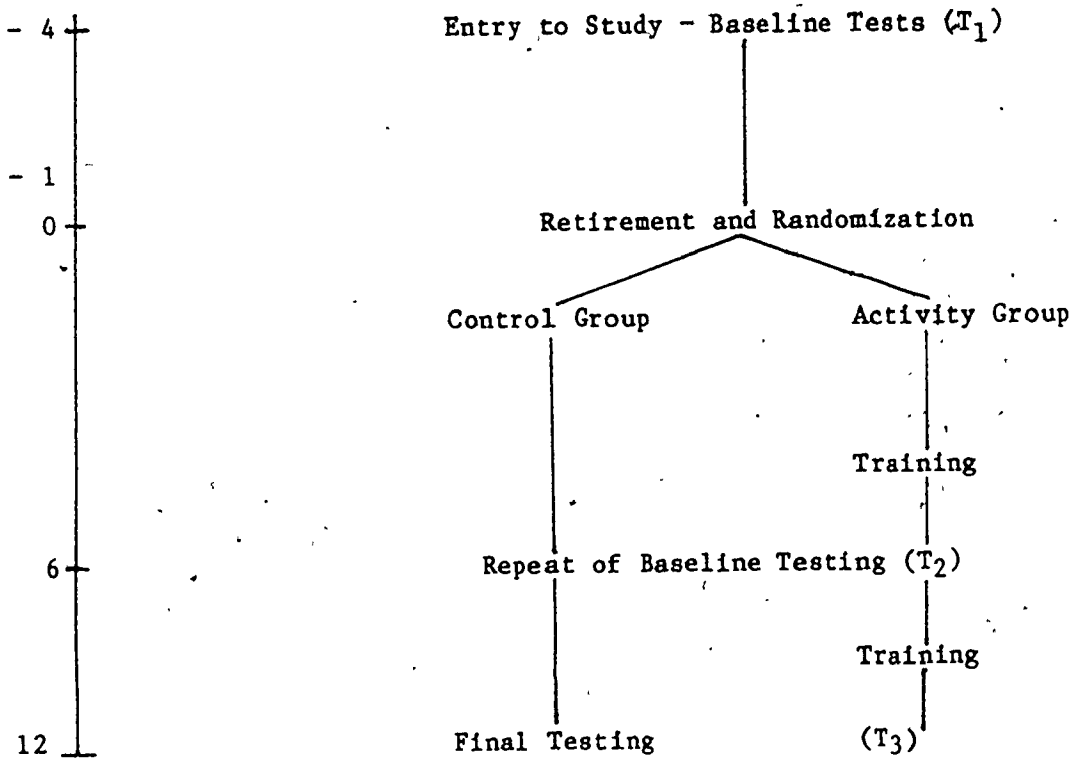
ST segment depression of 2 or more mm with a horizontal or downsloping ST segment resulted in a test halt. The physician also halted tests in which the ST segment was elevated 2 mm or more, T wave inversion was observed or premature ventricular contractions occurred more than 10 times per minutes (Cunningham and Rechnitzer, 1974).

Medication.

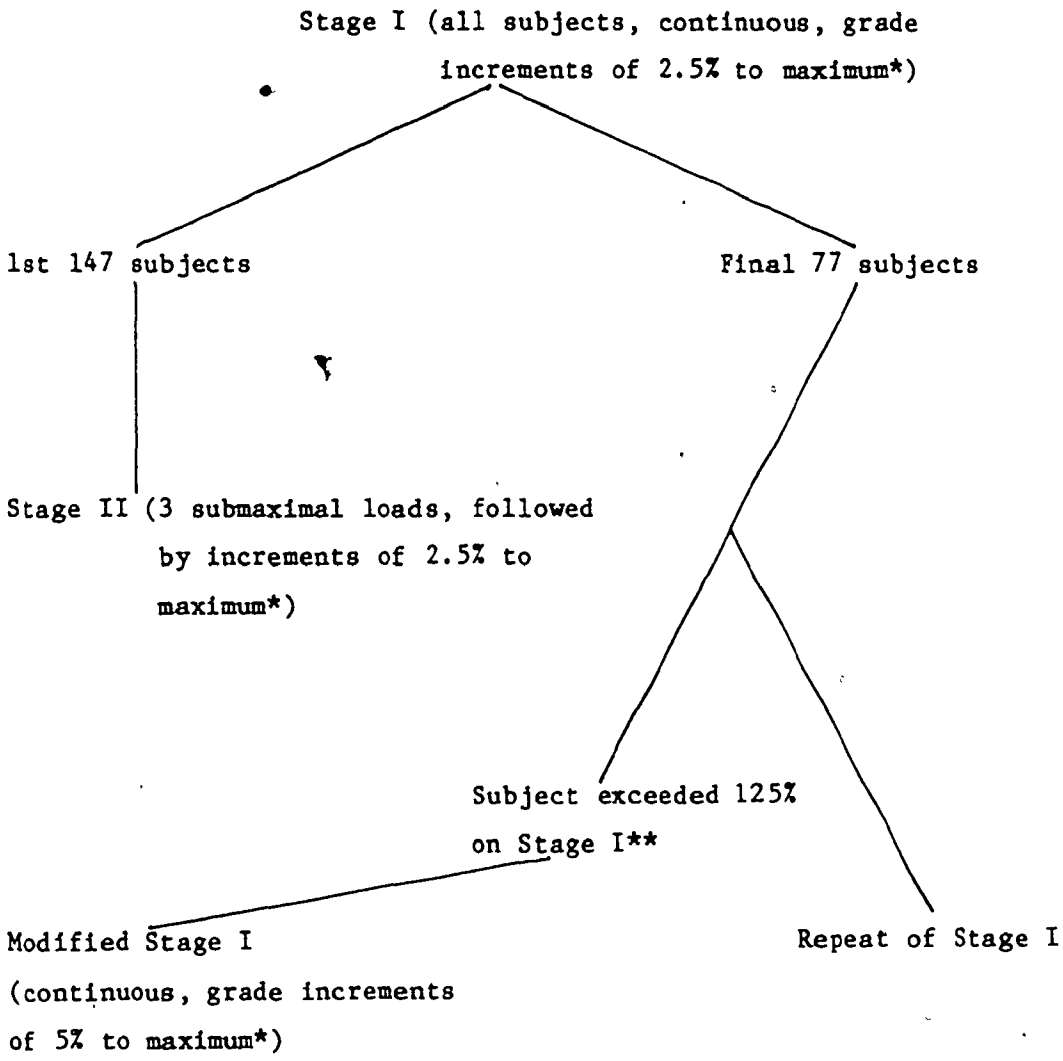
Subjects receiving β-blocking drugs were weaned from them over 72 hours. During the first 24 hour period drug dosage was reduced by 50%, then to 25% of the original during the following 24 hour period, and finally halted over the final 24 hours.

Study Protocol

Time (months)



Treadmill Test Protocols



* - if 20% grade achieved speed increased by 8 m/min.

** - protocol modified to equalize test duration.

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